TRABALHO FINAL

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Illuminated Micro-Catheter assisted Trabeculotomy: Literature Review

Lara Andreia Brito da Cruz Silva Dias

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I - ABSTRACT

Purpose: Review the literature of MAT for the treatment of pediatric glaucoma. Methods: Literature review from inception to January 2020 performed using an electronic database search on PubMed (MEDLINE) and Cochrane Central Register of Controlled Trials (CENTRAL). Data retrieved from the articles included patient's characteristics, IOP, glaucoma medication's number, surgical success rate, failure causes, intra and postoperative complications. Results: Eleven studies were included in the review, 8 were MAT case series and 3 were RCT, of which 10 were comparative studies (between MAT and goniotomy/CT/trab-trab). Five studies included only patients with PCG and six studies included patients with PCG and/or SCG. Analysis of 507 eyes of 423 patients were included, MAT was performed in 305 eyes. of which 197 eyes (64.7%) underwent complete canalization and 108 eyes (35.4%) only partial SC canalization. In 31 eyes (10.2%) MAT was not technically possible with conversion to CT. The average age at the time of surgery was 25.7±15.0 months and the mean time of follow was 13.0±8.5 months. Postoperative IOP and number of glaucoma medications at 24 follow-up months (11.5±3.4mmHg, 0.3±0.6 medications) were significantly lower in comparison to preoperative values (29.6±6.4mmHg, 2.0±0.9 medications). The average CS rate was 75.0% and 65.5% at12 and 24 months of follow-up, respectively, and the mean QS rate was 86.8% and 83.9%, respectively. In the eyes that underwent MAT, 46 failed, most of them (n =19 eyes, 41.3%) due to need for additional glaucoma surgery. The most common intra and/or postoperative MAT complication was hyphema. Conclusions: MAT achieved significant pressure-lowering effects with minimal complications in the early postoperative course (up to 24 months) and a reduction in medication use, in pediatric glaucoma (PCG and/or SCG), not only as an initial intervention but also in patients with previous surgeries. It can be successfully used to catheterize SC in most cases. It represents a reasonable choice of initial and repeat surgical treatment of pediatric glaucoma. Further research is warranted to determine the long-term success and safety of this procedure.

Key words: pediatric glaucoma, congenital glaucoma, intraocular pressure, 360º trabeculotomy, illuminated microcatheter.

I - RESUMO

Objetivo: Revisão da literatura da trabeculotomia assistida por microcateter iluminado (MAT) no tratamento do glaucoma pediátrico. Métodos: Realizou-se uma revisão da literatura até Janeiro de 2020, utilizando a pesquisa eletrónica na PubMed (MEDLINE) e Cochrane Central Register of Controlled Trials (CENTRAL). A informação de cada artigo for compilada com base na abordagem terapêutica, tendo sido depois avaliada e interpretada criticamente. A análise dos artigos incluiu características do paciente, pressão intraocular (PIO), número de medicamentos para glaucoma, taxa de sucesso cirúrgico, causas de falha, complicações intra e pós-operatórias. Resultados: Foram incluídos onze estudos na revisão: oito MAT casos-serie e três ensaios clínicos randomizados, dos quais dez são estudos comparativos (entre MAT e goniotomia/CT/trab-trab). Cinco estudos incluíram apenas pacientes com PCG e seis estudos incluíram pacientes com PCG e/ou SCG. Foi incluída a análise de 507 olhos de 423 pacientes, sendo que a MAT foi realizada em 305 olhos, dos quais 197 olhos (64.7%) foram submetidos à canalização completa e 108 olhos (35.4%) apenas a canalização. Em 31 olhos (10.2%), a MAT não foi tecnicamente possível ser realizada, sendo realizada conversão para CT. A idade média no momento da cirurgia foi de 25.7±15.0 meses e o seguimento médio entre estudos foi de 13.0±8.5 meses. A PIO no pós-operatório e o número de medicamentos aos 24 meses de pós-operatório (11.5±3.4mmHg, 0.3±0.6 medicamentos) foram significativamente menores que os valores pré-operatórios (29.6±6.4mmHg, 2.0±0.9 medicamentos). A taxa média de CS foi de 75.0% e 65.5% aos 12 e 24 meses, respetivamente e a taxa média de QS foi de 86.8% e 83.9% aos 12 e 24 meses, respetivamente. Nos olhos submetidos à MAT, 46 falharam, a maioria (n=19 olhos, 41.3%) devido à necessidade de cirurgia adicional. A complicação intra e/ou pós-operatória mais comum na MAT foi o hifema. Conclusões: A MAT obteve efeitos significativos na redução da PIO com complicações mínimas no pós-operatório precoce (até 24 meses) e redução no uso de medicamentos no glaucoma pediátrico (PCG e/ou SCG), não apenas como intervenção inicial, como em pacientes com cirurgias prévias. Pode ser utilizado com sucesso para cateterizar o canal de Schlemm na maioria dos casos. Representa uma escolha razoável de tratamento cirúrgico inicial e repetido do glaucoma pediátrico. Serão necessárias mais pesquisas para determinar o sucesso e a segurança a longo prazo deste procedimento.
Palavras-chave: glaucoma pediátrico, glaucoma congénito, pressão intraocular, trabeculotomia 360º, microcateter iluminado.

INDEX

ABBREVIATIONS

AC - Anterior Chamber

AL - Axial Length

CCT - Central Corneal Thickness

CS – Complete Success

CT – Conventional Trabeculotomy

DM - Descemet Membrane

GAT - Goldmann Applanation Tonometry

GATT – Gonioscopy-assisted transluminal 360º trabeculotomy

GDD – glaucoma drainage device

IOL – Intraocular Lens

IOP - Intraocular Pressure

JOAG - Juvenile-Onset Open Angle Glaucoma

M = Month

MAT – Microcatheter assisted trabeculotomy

MMC – Mitomycin C

N = Number

PAS - Peripheral anterior synechiae

PCG - Primary Congenital Glaucoma

QS – Qualified Success

RCT – Randomized Clinical Trial

RNFL – Retinal Nerve Fiber Layer Thickness

SC - Schlemm's Canal

SCG: Secondary Congenital Glaucoma.

SPG - Secondary Pediatric Glaucoma

TM - Trabecular Meshwork

Trab-Trab: combined trabeculotomy with trabeculectomy

UBM: Ultrasound biomicroscopy

WGA - World Glaucoma Association

II - INTRODUCTION

Glaucoma in children is a rare, potentially blinding condition characterized by elevated IOP with related damage to the eye and is caused by a diverse group of conditions. Clinical presentation can vary because, depending on the age of onset, elevated IOP can affect the whole eye and not just the optic nerve as in adults. The goal of the treatment is to provide a lifetime of vision if possible. Successful control of IOP is crucial in achieving this goal but can be challenging, especially when surgery is necessary. The correction of ametropia and amblyopia therapy is also vital to maximize visual function.[1]

Glaucoma from any cause in a neonate or infant classically presents with a triad of lacrimation, blepharospasm, and photophobia due to corneal edema from elevated IOP. These signs are not entirely specific but are very suggestive of glaucoma and may appear before the hazy cornea and characteristic buphthalmos become obvious. *Buphthalmos* refers to the ocular enlargement caused by elevated IOP. The potential for corneal enlargement usually ceases by the age of 3 years, although the sclera remains deformable until around 10 years of age. Moreover, as the IOP rises, Descemet membrane eventually ruptures, with one edge usually retracting as a scroll to form a ridge known as *Haab strae*. As the underlying endothelium is torn, localized or diffuse corneal edema results from aqueous influx into the stroma causing a sudden cloudiness. With successful lowering of IOP, corneal clouding typically begins clearing first in the periphery. Photophobia may still persist with normalization of IOP due to the Haab striae. Beyond the age of 3 years, children are more likely to present with progressive myopia, strabismus, or after having failed vision testing.[1]

Although medical therapy is still the mainstay for many types of pediatric glaucoma, surgery is much more frequently needed than in adult glaucoma for long-term control because of the refractory nature of the disease in children. [1]

II.A – Diagnostic Criteria and Classification of Pediatric Glaucoma

In 2013 the Consensus Group for Childhood Glaucoma from the WGA has developed the diagnostic criteria and a classification system from pediatric glaucoma (Figure 1). The **diagnosis** is made if two or more criteria are met including ocular hypertension, optic nerve cupping, Haab striae, increased corneal diameter or axial length and/or visual field defect.

Generally, this condition can be classified as: *primary* where there is only a developmental abnormality of the iridocorneal angle; and *secondary* where aqueous outflow is reduced by congenital or acquired ocular diseases or systemic disorders.[2]

Primary glaucoma in childhood can be defined as primary congenital glaucoma (PCG) or juvenile-onset open angle glaucoma (JOAG), depending on the age of disease onset and angle dysgenesis. The pathogenesis of the PCG is that of an isolated trabeculodysgenesis, which leads to a reduced aqueous outflow and raised IOP during the early years of life.

Secondary pediatric glaucoma (SPG) can either present at birth as a result of developmental ocular anomalies (nonacquired form) or develop later in childhood (acquired form). Conditions such as in iridocorneal dysgenesis: Peters anomaly, Axenfeld-Rieger syndrome, and aniridia are associated with the *nonacquired type* of secondary glaucoma in children. Common causes of the *acquired* secondary form include steroid induced, trauma, ocular inflammation, tumors, retinopathy of prematurity and following cataract surgery.[1]

II.B – Principles of Management

Any suspicion of glaucoma in a child should always be treated seriously and with urgency to minimize visual impairment. The aim of the initial assessment is to make a diagnosis of glaucoma and determine the type (primary or secondary) which is necessary in determining management.

It is important to begin the examination by assessing the patient's overall appearance and visual behavior including the presence or absence or nystagmus or strabismus and the determination of visual acuity and refraction. Subsequently IOP measurements should be undertaken. In children measuring IOP can be challenging because it can be influenced by many factors, e.g. type of anesthetic, instrumentation, corneal thickness and opacities. The reference standard for measuring IOP is with GAT. More recently, the iCare® portable rebound tonometer has become available for IOP measurement without the instillation of topical anesthetic drops in both supine and upright positions. It is well tolerated and is thought to have a similar reliability to TonoPen®, both of which have a tendency to overestimate IOP compared to GAT.[3,4]

In the **anterior segment examination,** the cornea must be examined for the presence of posterior embryotoxon, edema, opacities and Haab striae. Excluding primary corneal pathology is important, and a useful finding is the absence of corneal or ocular enlargement. The *corneal diameter* should be measured, and it was considered abnormal if horizontally ≥11 mm in a newborn and ≥ 12 mm in an infant <1 year and ≥13mm after 12 months of age. Serial corneal diameter measurements are useful in monitoring glaucoma progression until the age of 3 years. An increasing corneal diameter may indicate inadequate control of IOP requiring further treatment.[42] CCT influences the accuracy of tonometry. Patients with PCG and JOAG have thinner corneas and in theory a tendency for under reading the IOP. Conversely, an increase in corneal thickness, as is found in patients with aphakia and aniridia, may lead to an overestimation of IOP. Regardless of corneal thickness, the emphasis remains on the optic disc appearance.[1] Detecting iris or pupil abnormalities or co-existing lens opacities is important as the latter may require treatment and influence the choice of glaucoma surgery.[1] Gonioscopy is crucial in making the correct diagnosis, which determines the most appropriate operation and prognosis.

Finally, the **posterior segment examination** should be performed. The appearance of the optic disc is by far the most important and sensitive parameter for both diagnosis and progression of glaucoma, as it is influenced neither by anesthesia nor the effect of growth. *Richardson*[2] noted a cup:disc ratio (C/D) of greater than 0.3 in only 3% of 468 *normal* Caucasian newborn eyes, in contrast to *Shaffer* who found a C/D of greater than 0.3 in 61% of 85 eyes in infants less than 1 year with congenital glaucoma.[3] A C/D > 0.3 in a Caucasian infant less than 1 year or >0.5 in a child and disc asymmetry should greatly increase suspicion of glaucoma. An increase in disc cupping is definite evidence of poorly controlled glaucoma and the need for further treatment, regardless of IOP measurement obtained. Disc cupping in children can be reversible if IOP reduction occurs before irreversible nerve atrophy, and it is more likely in the younger the child. It is thought to represent a "pre-laminar" phenomenon where reversible laminar bowing is associated with compression and stretching of the pre-laminar neural tissue. Once the IOP is normal, the compression is relieved allowing the laminar to move anteriorly, "filling in" the cup. However, despite disc cupping reversal, retinal nerve fiber layer thinning may persist postoperatively.[7] The remainder of the fundus should be examined for any associated abnormalities such as foveal hypoplasia associated with aniridia, choroidal hemangiomas in Sturge–Weber syndrome, and pigmentary retinopathy associated with rubella.[1]

Axial length (AL) measurement with ultrasound is useful for baseline assessment; if it is outside normal limits it is strongly suggestive of glaucoma. Serial AL can be valuable in children for detecting progression when the eye is still distensible. In glaucoma, AL measurements are usually asymmetrical, in contrast to megalocornea and normal eyes. There is usually a decrease in AL following successful lowering of IOP.

Visual fields are usually possible around the age of 7–8 years, but there is a learning curve. Visual field defects must be reproducible, so defects must be confirmed by repeating the test. Furthermore, the defects must correspond to the optic disc appearance. OCT may be used since a young age to detect and monitor RNFL and macular ganglion cell layer thinning.[8]

II.C - Treatment of Pediatric Glaucoma

Managing glaucoma in childhood is one of the greatest challenges in the field of glaucoma. Medications play a vital role in management, as they are first-line therapy for most glaucomas; however, sustained efficacy is less likely in neonates and infants, especially those with PCG. Medications are frequently needed to lower the IOP before surgery and are often required as adjunctive therapy after partially successful. Most children with glaucoma will require surgery in their lifetime. However, surgery is challenging, largely because of its greater potential for failure and complications as compared to adults.[1] No treatment is curative, so lifelong follow-up is necessary to ensure IOP control and to detect complications, which can occur at any time, even after years of stability. Furthermore, parents and, later, patients should be warned that minor blunt trauma in buphthalmic eyes may result in severe visual loss. Protective eyewear should be recommended, especially in monocular patients. The first line treatment for children includes prostaglandin agonists, carbonic anhydrase inhibitors and beta-blockers. In young children (<8 years-old) alpha-adrenergic agonists, such as brimonidine, can cause central nervous system depression with resultant somnolence, hypotension, bradycardia, and respiratory difficulty, so this class of hypotensive drops is contra-indicated.[1]

Goals of the Surgery

Although for every glaucoma procedure the most immediate objective is the reduction of harmful elevated IOP, in children other aims need to be kept in mind when deciding which procedure to perform and when to do it. With children we are running against time because the sooner the child develops clear media, improved visual acuity and binocularity, the better. It is well known that in spite of adequate normalization of IOP, many elements hamper the development of a normal vision in these children; however, aiming at preserving or restoring the best possible visual function is an important final goal.[3,4]

Glaucoma surgery is classified in four broad groups: 1) angle surgery, 2) non penetrating glaucoma surgery, 3) glaucoma drainage devices and 4) LASER.

1.1 Angle Surgery

For pediatric glaucoma the most commonly performed angle surgeries are goniotomy (conjunctival sparing) and trabeculotomy (non-conjunctival sparing). Both procedures presumably work by allowing a more direct access of aqueous humor into Schlemm's canal and the outflow system. [1,5] Both types of angle surgery have been shown to be effective, there is a general preference to use goniotomy in milder cases with clear corneas and trabeculotomy and/or combined trabeculotomy with trabeculectomy (trab-trab) in mild-to-severe cases with opaque corneas (if the cornea is cloudy enough to preclude a safe goniotomy or when the surgeon prefers this technique due to prior training or more experience with the procedure even when the cornea is clear).

Table 1 illustrates the comparison between the different Angle Surgery Techniques for Pediatric Glaucoma.

1.1.1 Goniotomy

Goniotomy is the oldest procedure described for treating congenital glaucoma. Although initially used by *De Vincentis*, in 1893, for all types of glaucomas, *Barkan* is credited by combining it with gonioscopic view, including direct visualization of the angle and giving a detailed description of the procedure and reporting its successful use in congenital glaucoma in 1938. Modifications allowed to combine goniotomy with the use of the surgical microscopes, which were introduced into ophthalmology in the early 1950's, but routinely used in large eye institutions dealing with this disease (such as Moorfields Eye Hospital) until the late 1960's.[3] It remains one of the most widely used surgeries for the treatment of the pediatric glaucomas because of its efficacy and low complication rate.[3]

Goniotomy has the advantages of being brief in execution and atraumatic procedure in experienced hands, and it completely spares the conjunctiva so that the success of future filtration surgery will not be compromised. Although it requires considerable experience and it is surgically challenging. A good view of the angle is paramount and visualization can be improved in some cases with preoperative systemic carbonic anhydrase inhibitors, corneal epithelial removal, or the use of an endoscope. [1]

The technique consists of performing an incision of trabecular meshwork with a 25G goniotomy knife (MVR blade) by direct visualization of the angle with a gonio lens (*Koeppe*, *Barkan*, *Swan-Jacobs* and Ritch).[3] The trabecular meshwork is engaged just posterior to Schwalbe's line, and the knife is used to make a circumferential incision for 4 to 5 clock hours. Care must be taken not to incise too deeply and damage the outer wall of Schlemm's canal.

Often, a cleft with exposure of less pigmented tissue is observed as the incision is made, with widening of the angle and posterior movement of the peripheral iris.[5] Goniotomy can only treat 100-120º of the angle at each sitting. Hence, repeating this procedure is often undertaken to maximize its surgical results when deemed necessary.[1]

Complications

Goniotomy is commonly complicated by hyphema, which usually resolves without intervention over the first postoperative week. Other complications are rare but include iridodialysis, peripheral anterior synechiae, cyclodialysis, injury to the crystalline lens, retinal detachment and endophthalmitis.[5]

Outcomes

Repeat procedures in untreated portions of the angle may improve pressure control, although there are no reliable data correlating the number of degrees treated and surgical success. However, overall the success of goniotomy has been reported to attain 80–90% **in** children with PCG who present between 3 months and 1 year of age. In children who present at birth or after 12 months of age, the success rate of goniotomy decreases to 30–50%.[2,5,6] In Arab Countries the success rate of goniotomy is low (~13-52%), therefore Trab-Trab plus mitomycin C is usually the primary procedure of choice.[3]

1.1.2 Trabeculotomy

Trabeculotomy has historically shown high rates of success for pediatric glaucoma.[7] Accurate localization of Schlemm canal is the key to successful trabeculotomy. However, abnormally stretched limbal anatomy in buphthalmic eyes makes it difficult to identify and it may not be found at all in 4–20% of patients, especially if the AC is inadvertently entered before the canal is found.[9] Controversy regarding which was a better initial procedure (trabeculotomy versus goniotomy) exists since the introduction of trabeculotomy and remained for a long time, with some authors arguing that trabeculotomy had a better success rate as a single procedure than goniotomy.[3]

Although trabeculotomy ab externo has the disadvantage of requiring a conjunctival incision, its main advantage is that it can be performed easily in eyes with corneal opacity. In addition to standard trabeculotomy, there are 2 main variations of trabeculotomy surgery: suture trabeculotomy and illuminated microcatheter-assisted trabeculotomy.

Conventional trabeculotomy is performed with metal trabeculotome instruments, enabling approximately 180º of the Schlemm canal to be opened at a single surgical session.[5] *Burian and Smith* first described performing 360º suture trabeculotomy in cadaveric eyes in 1960.

Then it was modified by *Harms* (1966) and *Dannheim*, and *McPherson*.[5] Later, in 1966, *Harms* modified the technique by dissecting a superficial scleral flap similar to the one used in trabeculectomy and then making the radial incision to identify Schlemm's canal and opening it with a modified instrument (Harm's trabeculotome) which had two parallel arms, one to open Schlemm's canal and the other one to guide externally the direction of the trabeculotome.[6]

Complications

As with goniotomy, a frequent complication of trabeculotomy is hyphema, which was mostly self-limited and does not require intervention. Other less frequent complications include inadvertent filtering blebs, choroidal detachment, iridotomy, injury to the crystalline lens, creation of a false passage into the AC, cornea, or suprachoroidal space, and stripping of DM.[9]

Outcomes

Success rates of trabeculotomy have been reported in the range of 73–90% in congenital glaucoma. As with goniotomy, success rates decrease in PCG that presents at birth or after 12 months of age, as well as in patients with infantile-onset glaucoma associated with ocular and/or systemic abnormalities or aphakic glaucoma.[2,5]

1.1.3 Modifications to the Goniotomy and Trabeculotomy Procedures

A) 360º Trabeculotomy with suture

Beck and Lynch refined trabeculotomy's technique by using 6-0 prolene suture threaded around the entire length of Schlemm's canal, using 1 or 2 sclera incisions. A direct communication between the AC and Schlemm's canal is created by cannulating the Schlemm's and then tearing through the trabecular meshwork into the AC. The entire angle is incised, thus avoiding multiple procedures that may be needed in some cases using conventional trabeculotomy or goniotomy, both of which treat only about a third to a half of the angle. Although elegant, this 360º suture technique can be challenging, with difficulties most often including inability to thread the suture to a full 360º angle and an occasional suprachoroidal placement of the suture.[9] As prolene is very rigid with a greater potential for damaging the intraocular structures, more recently the same technique using a 4-0 or 5-0 nylon has been used. The progress of the suture can be appreciated through use of a gonioprism.[10,11] Success rates of 87–92% have been reported in cases of PCG < 12 months of age. In childhood glaucoma with a poor prognosis (PCG at birth or after 12 months of age, previously failed goniotomy surgery, aphakic glaucoma, infantile-onset glaucoma with associated ocular/systemic anomalies) 360° suture trabeculotomy has a 2-year success rate of 58–62%.[1]

B) 360º Trabeculotomy assisted with illuminated microcatheter

In 2010 *Sarkisian*[2] was the first to describe the technique of a **360º trabeculotomy** using an illuminated flexible microcatheter (iTrack, Ellex, Menlo Park, CA, USA). The lighted tip to guide the catheter minimizes potentially devastating inadvertent misdirection into the suprachoroidal or subretinal space by verification of the microcatheter location within Schlemm's canal.

The microcatheter has a 200µm diameter shaft with an atraumatic distal tip of approximately 250µm in diameter; it has a lumen with a proximal luer lock connector through which ophthalmic viscosurgical device (OVD) may be delivered. Therefore, this technique has the additional advantage of allowing viscodilation of the SC while it is cannulated (Figure 2).

B1) Ab externo Surgical Technique[2]

Beneath a 5mm superonasal conjunctival peritomy, Schlemm's canal was accessed by creating a 4.0x4.0mm flap scleral dissection just posterior to the limbus followed by a radial incision to reveal Schlemm's canal. After creating a small peripheral limbal paracentesis with a 15º blade, 2 tying forceps were used to grasp the microcatheter, placing the tip in alignment with the canal, and the device was advanced into the canal. The light beacon at the tip of the microcatheter allows visualization for more accurate placement of the device. When catheterizing the canal, the microcatheter has a lumen for fluid delivery for SC viscodilation, the general protocol for injection is approximately 4 to 6 mg of OVD injected every 2 clock hours of advancement using the OVD injector.

If a 360º catheterization is achieved, each end of the microcatheter is drawn like a purse-string to gently garrote the entire canal inward. If unable to complete a sufficient trabeculectomy, a Harms trabeculotome (Rumex Microsurgical Ophthalmic Instruments, St. Petersburg, FL) should be used to rupture as much of the canal wall as possible. The procedure is completed by closure of the superficial flap and conjunctiva to ensure a water-tight seal that would prevent the formation of a filtering bleb (Figure 3).

B2) Ab interno Surgical Technique[3]

A 23G needle paracentesis is placed in either the supero or infero-nasal quadrant and the AC is filled with OVD. A temporal paracentesis is created with a 15º blade. The microscope and the patient's head should be oriented to allow proper visualization of the nasal angle with a Swan-Jacob goniolens. A 1-2 mm goniotomy is created in the nasal angle with a microsurgical blade (25G MVR) through a temporal paracentesis. Microsurgical forceps (MST handle and

MST MH 23G) are then used to grasp the microcatheter within the AC. The distal tip of the microcatheter is inserted into the SC at the goniotomy incision. The microsurgical forceps are used to advance the catheter through the canal circumferentially 360º within the AC. The progress of the microcatheter is noted by observing the illuminated tip. The distal tip of the microcatheter is advanced in the canal until it reemerges at the opposite side. Upon retrieving the distal tip, the catheter tip is externalized from the temporal corneal incision creating the first half of the 360° trabeculotomy. Then, traction is placed on the proximal aspect of the catheter, thus creating a 360° ab interno trabeculotomy**.** The OVD is then removed from the AC, a 15-40% AC filled with viscoelastic is instilled to help tamponade bleeding from the canal and protect against immediate postoperative hypotony.

In certain cases, the microcatheter cannot be passed 360º in one direction and stops at around 180-270º. In these cases, a limited trabeculotomy is created by cutting down (*ab interno*) over the catheter at the stopping point. The distal end is retrieved and externalized, thus creating a 180-270º trabeculotomy. The microcatheter is then passed in the opposite direction through an additional 23G needle incision and the remaining trabecular tissue is cleaved.

B3) Ultrasound biomicroscopy – UBM[12]

High-resolution UBM can be utilized to visualize the amount of distention placed on TM (Figure 4). This might be useful to correlate the TM distension and the IOP results. A semiquantitative grading scale was created to quantify the distension of the TM on a scale of 0 to 3 based on exemplary images (Figure 5), with 0 equaling no distension and 3 representing maximum distension. UBM images are obtained using a system designed for intraoperative and office-based anterior segment imaging (iUltrasound, iScience Interventional) to characterize preoperative and postoperative anterior angle morphology. Of interest were postoperative images collected for all 4 quadrants of the operative eye to assess viscodilation of Schlemm's canal and distension of the trabecular meshwork from the tensioning suture. There is a substantial decrease in IOP from mean baseline in eyes with minimal or no trabecular distension (grade < 0.5) and a greater one in eyes with measurable distension (grade > 0.5).

C) Gonioscopy-assisted transluminal 360º trabeculotomy (GAAT)

Recently a minimally invasive ab interno trabeculotomy was described, termed gonioscopy-assisted transluminal trabeculotomy (GATT). *Grover and colleagues*[11] introduced this procedure in 2018. A goniotomy is created in the nasal angle using a 25G MVR blade. A 5-0 prolene suture (Ethicon) or microcatheter (iTrack) is inserted into the AC (Figure 6).

Microsurgical forceps are then used to direct the distal tip of the microcatheter into Schlemm's canal at the goniotomy site. Within the anterior chamber, the microsurgical forceps are used to advance the catheter through the canal circumferentially 360º. The distal tip of the catheter, once it has circumnavigated the entire canal, is retrieved and externalized, thus creating a 360º trabeculotomy (Figure 7).

Although only a few studies were published reporting the surgical success of GAAT, it has shown success in decreasing both IOP and number of glaucoma medications in primary, juvenile and secondary open-angle glaucoma, including uveitic, steroid-induced, traumatic, pigmentary, and pseudo exfoliation. GATT may even be an effective and safe option for patients with refractory glaucoma who have undergone previous incisional surgery (trabeculectomy, glaucoma drainage device, trabectome, or endoscopic cyclophotocoagulation).[13]

Smith et al. described a proposal of modification to the original GATT procedure by replacing the initial goniotomy incision of the GATT procedure with an ab interno trabeculectomy performed with the trabectome (trabectome-initiated gonioscopy-assisted transluminal trabeculotomy -TIGATT). This is an easier method of performing GATT because it provides clear visualization into Schlemm's canal and eases the passing of the microcatheter into the canal (Figure 8). The trabectome handpiece (NeoMedix Corporation, Tustin, CA, USA) is inserted into the AC via the temporal incision and used to ablate 90º of the nasal trabecular meshwork. The rest of the procedure is completed as described in the original GATT procedure.[14]

1.2 Trabeculectomy

Trabeculectomy, involves a surgically formed pathway for aqueous humor between the AC and the subconjunctival space. One of the main indications for trabeculectomy is failed angle surgery. It may be the primary procedure of choice when: the surgeon has no or limited experience with angle surgery; the patient is unlikely to respond sufficiently to angle surgery (very early or late presentations); very low target pressures are required (improved cornea clarity, advanced disc cupping); and for most secondary glaucomas. One disadvantage of this technique is that the superior conjunctival area is utilized, and even after successful surgery, with a normal life expectancy, there is a high likelihood that a significant proportion of these patients will need further surgery within their lifetimes.

The decision to perform trabeculectomy with antimetabolites in a child is difficult and requires consideration of several factors. Age of the child is a major consideration, as older children tend to have a higher success rate and may be able to cooperate more readily with postoperative management such as monitoring for bleb leaks and suture release. Older children may also be able to communicate symptoms of bleb-related infection and thus have a higher likelihood of appropriate treatment.[5] Severity and duration of glaucoma are other negative predictive factors for success with either surgery.[6] Phakic status, avoidance of contact lens use, and social support are also factors to consider in surgical decision making.[5]

Complications

Early complications are related to hypotony (shallow or flat AC, hypotony maculopathy, choroidal effusion, suprachoroidal hemorrhage) and late complications are associated with thin avascular, cystic blebs prone to leakage and potentially blinding infection (including blebitis/endophthalmitis), encapsulation of the bleb with resultant IOP elevation and increased risk for cataract formation. The most striking difference in complication rates after surgery when comparing the adult and pediatric populations is the rate of infection after trabeculectomy which are substantial higher, up to 6.7%.[9] Another potential difference in trabeculectomy postoperative complications between adults and children is the healing response to overfiltration. Although hypotony (0%-14.5%) and shallow or flat AC (3.0%-30.0%) are common in children, some authors have suggested that the vigorous healing response in children may reverse overfiltration quicker compared with adults.[9]

Outcomes

In pediatric patients, the success rate of trabeculectomy without adjunctive antimetabolites is 30–35%. With the use of adjunctive antimetabolites, the cumulative success rate at 2 years vary between 59–90% and reduces to 51-58% at 5 years.[1,3,9]

1.2.1 Combined Trabeculotomy and Trabeculectomy (Trab-Trab)

This technique was first described by *Maul et al* in 1980.[1] Studies have suggested that the principal argument for combined Trab-Trab is a higher chance of success with a single operation.[3] The intended mechanism of action for combining these two procedures is to gain access to dual outflow through Schlemm's canal and/or the trabeculectomy fistula. In the treatment of eyes with PCG, this technique marries the ideology of treating the site of primary pathology (i.e. the angle) with the hope of achieving maximal surgical survival in a primary filtration surgery. [3] Mostly the technique is used in children with poor prognosis childhood glaucoma or prior failed angle surgery. Antimetabolites such as MMC and 5-FU have also been used at the site of the scleral flap prior to flap dissection.[5]

Complications

Most ones are similar to the ones described in trabeculotomy and trabeculectomy sections.[3]

Outcomes

Trab-trab has been shown to be potentially more effective than either procedure alone in cases of severe PCG, although there has been a lack of prospective comparative data thus far to demonstrate this. The results of this procedure have been mostly reported in Middle Eastern and Indian populations, where it was used preferentially because it was felt that congenital glaucoma did not respond as well to angle surgery as previously described in western populations.[1,3,5,9,15]

1.3 Non-Penetrating Glaucoma Surgery

Viscocanalostomy and deep sclerectomy are newer operations for glaucoma that aim to lower IOP by enhancing the natural aqueous outflow channels, while reducing outflow resistance located in the inner wall of the SC and the juxtacanalicular TM. Both procedures involve fashioning a partial-thickness scleral flap, removing a second layer of sclera deep to the initial flap that involves deroofing of the SC, and exposing DM (Figure 9). Aqueous is then allowed to percolate through the intact DM window into the intrascleral space. [1] In small series deep sclerotomy has a reported success rate between 50-70%. Because of the nonpenetrating nature of the surgery, complications commonly seen after trabeculectomy surgery, such as early-hypotony, cataracts, and long-term complications of filtering blebs including leaks and infection, may be reduced or avoided. Difficulties with these procedures in children are that they have a thinner and more elastic sclera and variable anatomical features, and it is not always possible to identify Schlemm's canal, all of which make a procedure already technically demanding, even more challenging and more likely to be performed at highly specialized centers in treating this condition. [3]

1.4 Glaucoma Drainage Device

For refractory cases after angle surgery the next step would be glaucoma drainage device (GDD) implantation. The most common GDD used currently are the Ahmed glaucoma valve (AGV, New World Medical Inc., CA, USA) with unidirectional flow restriction, which theoretically reduces the risk of early hypotony and the Baerveldt glaucoma implant (BGI, plate 250mm^2 and 350mm^2), which is an unrestricted implant (AMO Inc., IL, USA) and so requires additional measures to minimize early hypotony.[1,16-19] Success rates in published studies of GDDs are difficult to compare due to differences in pediatric glaucoma etiologies and devices.

Recently a new technique has been described for using the XEN gel stent (Allergan, Dublin, Ireland) as a flow restrictor for the Baerveldt tube. Therefore, precluding early postoperative hypotony and reducing corneal endothelial trauma.[20] Furthermore a new GDD was introduced, the Paul glaucoma implant (Advanced Ophthalmic Innovations Ltd, Singapore). This device has the advantage of having a large thin plate as the BGI, however the tube's internal lumen diameter was reduced to one third of the size (125 vs 300µm Paul vs BGI). In theory this might also reduce the risk of corneal endothelial trauma and early postoperative hypotony.[48]

Outcomes

At 1–2 year follow–up, many studies report a success of around 80% and this falls to around 50% in the longer term.[36-39] When debating which GDD performs best in children—there is no clear superiority of one type of GDD versus another, however the BGI may provide slightly better long- term IOP control but the AGV fewer short term complications. [36-39]

Complications

One of the most common and sight-threatening complications of GDD surgeries in children is postoperative hypotony. The risk may be mitigated by reducing aqueous flow with external ligation of both flow-restricted and unrestricted implants. Other than hypotony, a wide range of complications may occur, including lens touch with cataract formation, corneal touch with corneal decompensation, and iris touch with persistent iritis or dyscoria. Moreover, tube migration either into the anterior chamber or posteriorly out of the anterior chamber has been documented. Tube obstruction from iris, vitreous, hemorrhage, and fibrinous or inflammatory membrane can also occur, whereas tube erosion and exposure can lead to infections and endophthalmitis. In some cases, GDDs may cause cosmetic or eye motility issues. Tube exposure is an important complication in the long term. Early recognition of endophthalmitis is extremely important, and most will require emergency removal of tube and plate in order to prevent further proliferation of the infection, which can lead to total loss of sight. GDD can reduce endothelial cell density over time, leading to corneal decompensation. Fibrosis and encapsulation around the plate remain the main reasons of GDD failure. In contrast with trabeculectomy, the advantage of reducing fibrosis with anti-scarring agents has not been established in GDD surgeries in pediatric eyes. However, some authors support that after failed GDD surgery, repeat GDD surgery with MMC may be successful. After GDD failure, the introduction of topical glaucoma medication is considered to be the simplest and lowest risk option. Alternatively, needling or surgical revision of the bleb over the plate (capsule excision) can be considered.[36-39]

1.5 CYCLODESTRUCTION

Cyclodestruction reduces aqueous production. Initially, cyclotherapy demonstrated poor-long term outcomes. In the past years, it has been replaced by less destructive LASER cyclophotocoagulation. Specially the transcleral diode laser (810nm) in comparison to the Nd:YAG KTP laser (532nm), as it is better tolerated and with fewer complications.[4]

A major drawback of the transcleral approach is ensuring accurate laser placement in buphthalmic eyes with distorted landmarks and hence difficulty in titration of laser energy. Endoscopic diode laser allows precise treatment of the ciliary processes, but the disadvantage is it requires an intraocular approach and caution is suggested in phakic patients. Transscleral diode laser with transillumination of the eye to improve the accuracy of laser placement, and avoiding areas of pigmentation, hemorrhage, and scleral thinning. If future GDD surgery is planned, the supero-temporal quadrant should be avoided to prevent future scleromalacia. Diode laser should be avoided in children with uveitic glaucoma due to poor outcomes and risk of chronic hypotony.

Common indications include treating blind, painful eyes or those with poor visual potential; if surgery is technically difficult or impossible for example, severely scarred conjunctiva or if there are significant ocular abnormalities. Occasionally it may be useful as a temporizing measure, for example, an acute presentation of significantly elevated IOP as occurs following trauma, during the hypertensive phase of an Ahmed implant in aphakic/pseudophakic eyes or when a definitive procedure must be delayed for example, fellow eye has undergone major surgery. [4]

Complications

Complications associated with diode laser include: hypotony, significant uveitis, phthisis, conjunctival burns, uveitis, scleromalacia, scleral perforation, cataract, retinal detachment, and loss of vision especially in eyes with two or more treatments or in eyes with pre-existing poorvision.[3]

Outcomes

Short-to-medium term outcomes of transscleral diode laser quote over 50% success but with a high re-treatment rate and a continuation of medical therapy. Endoscopic diode achieves similar results with a lower re-treatment rate.[3]

II.D – Postoperative Care and Follow-up

After surgery, all patients should be given topical broad-spectrum antibiotics and topical steroids. The main goals are to prevent infection, controlling inflammation and preventing a steroid IOP response.

The patient's IOP should be treated during the postoperative period according to the surgeon's discretion.

Postoperative visits: 1 day, 1 week, 2 to 3 weeks, 1 month, 3 months, 6 months, and thereafter every accordingly to patient's evolution. During follow-up visits, the following data should be evaluated: visual acuity, refraction, IOP, number of glaucoma medications, anterior and posterior segment evaluation, surgery-related complications, gonioscopic findings and axial lengh.[11] If a reliable exam and IOP measurement cannot be obtained in clinic, exam under anesthesia should be performed.[3]

In general, for all glaucoma procedures potential **early postoperative complications** include: hypotony (shallow/flat AC, wound leak, choroidal detachment), hyphema, corneal edema, aqueous misdirection, suprachoroidal hemorrhage, vitreous hemorrhage, decompression retinopathy, and cystoid macular edema. Potential **late postoperative complications** included: persistent corneal edema, corneal ulcer, dysesthesia, blebitis (if patient had previous trabeculectomy), chronic/recurrent iritis, choroidal effusion, cystoid macular edema, hypotony maculopathy, persistent diplopia, endophthalmitis, retinal detachment. [1]

III - METHODS

A literature review of articles published from January 1953 (inception) to January 2020 was performed using PubMed (MEDLINE) and Cochrane Central Register of Controlled Trials (CENTRAL), searching for articles which mention therapeutic results of surgical interventions for glaucoma on patients with pediatric glaucoma in an attempt to answer the question "Which therapies for pediatric glaucoma have the longest maintained efficacy with least incidence of adverse reactions?". Search keywords included congenital glaucoma, pediatric glaucoma, trabeculotomy, iTrack and illuminated microcatheter, were used in this search, with different combinations in order to obtain the maximum of available articles. Studies were initially screened by the title and abstract and submitted to the full-text assessment if eligible. Then, all articles were read with the relevant information being compiled based on therapeutic intervention and were critically assessed and interpreted.

A) Types of studies

There were two types of studies included in this review: eight were case series[11,21-23,26-29] and three were randomized clinical trials (RCT).[7,24,25]

B) Types of participants

The participants included were pediatric patients (<18 years old) with childhood glaucoma with uncontrolled IOP. In most studies, patients with previous glaucoma surgery were excluded from analysis,[11,24,25,27,28] and in five studies these patients were in the analysis.[21-23,26,29]

C) Types of interventions

The intervention of interest was ab externo 360º trabeculotomy assisted with illuminated microcatheter.[7,11,22-29] Studies with comparison interventions could be either goniotomy,[11] conventional trabeculotomy,[21,23-25,27] or combined trabeculotomy-trabeculectomy.[7]

D) Types of outcome measures

The main clinical outcome in most studies was IOP. The target IOP was different between studies: ≤12mmHg (n = 1)[25], ≤15mmHg (n = 1)[7] , ≤18 mmHg (n = 3)[22-24], ≤21 mmHg (n=1)[21], ≤21 mmHg and a 30% reduction of IOP (n=4) [11,26,27,29] and ≤22 mmHg and a 30% reduction of IOP (n=1).[28]

Complete success was considered if target IOP was achieved without any topical medications and qualified success if with or without it.

IV – RESULTS - COMPARATIVE STUDIES

We included 11 studies in this review (Table 2 details studies characteristics):

- comparative studies between MAT with goniotomy: 1 [11]
- comparative studies between MAT with conventional trabeculotomy: 5 [21,23-25,27]
- comparative studies between MAT with trabeculotomy-trabeculectomy: 1 [7]
- MAT case series: 4 [22,26,28,29]

A summarized comparison regarding demographics, glaucoma etiology, type of intervention, follow-up, success (complete and qualified) rate, failure causes, IOP, medications and complications are detailed in Table 2 and Table 3.

A) Patients Characteristics

A1) Demographics

In total 423 patients and 507 eyes were included in these studies, of which 305 eyes (74.9%) underwent microcatheter assisted ab externo trabeculotomy (MAT). The average age at the time of surgery was 25.7±15.0 months (4m-18y). There was higher male preponderance with a mean of 66% (56-91).[11,21-29]

A2) Childhood glaucoma type

Five studies included only patients with primary congenital glaucoma (PCG).[7,21,23,25,26] Six studies included patients with PCG and/or secondary congenital glaucoma (SCG), which more commonly included glaucoma associated with aphakia, aniridia, Axenfeld-Rieger, Sturge-Weber and Rubinstein-Taybi syndrome.[11,22,24,27] One study included patients with PCG, SCG and JOAG,[29] and another study compared aphakic glaucoma patients in one group and JOAG in the other group.[28]

A3) Baseline characteristics

The mean preoperative IOP was 29.6±6.4mmHg (21-36)[11,21-29] under a mean number of 2.0±0.9 (0-4)[11,22-24,26-28] glaucoma medications. Average follow up between studies was 13.0±8.5 months (7-31).[21-24,26-29]

B) Surgical Success

Success rate wasn't uniformly reported between studies included in this analysis, from the 11 ones, 8 performed Kaplan-Meier survival analysis (at different time points)[11,21,23,24,26-29] and the remaining 3 studies reported success rate at around 12 months of follow-up.[7,22,25] Details for qualified and complete success are presented in Table 4 and Table 5.

The average **complete success rate** was 92.9% (83-100) at 1 month of follow up,[23,24,26,27,29] 81.4% (70-91) at 3 months, [23,24,26,27,29] 75.0% (62-91) at 6months,[23,24,26-29] 75.0% (33-87) at 12 months[11,21-29] and 65.5% (53-80) at 24 months.[21,23,24,28] The mean **qualified success rate** was 95.2% (84-100) at 1 month follow up, [23,24,26,27,29] 91.1% (90-93) at 3 months,[23,24,26,27,29] 89.4% (86-91) at 6months,[23,24,26-29] 86.8% (44-100) at 12 months,[11,21-29] and 83.9% (76-90) at 24 months.[21,23,24,28] The **mean survival time for MAT** was reported in two studies, with an average of 20.1±1.5 months (19-21).[23,24]

Regarding the **postoperative IOP control** and **number of glaucoma medications**, after MAT the average IOP was 13.4±3.7 mmHg (10-19)[7,23-25,27,29] with 0.4±0.9 (0-1) medications[23,27] at 6 months, 13.7±3.5mmHg (9-21)[7,11,22-27] with 0.4±0.6 (0-1) medications[11,22,23,26,27] at 12 months and 11.5±3.4mmHg (9-13)[23,24] with 0.3 ± 0.6 (0-1) at 24 months follow up.[23]

In this review in the eyes that underwent MAT, 46 failed, however only in 35 eyes the motif for failure was disclosed. In the studies where data was available, 19 eyes (41.3%)[22-26,28] failed due to need for additional glaucoma surgery, 13 eyes (28.3%)[7,21,23,28] due to poor IOP control, 2 eyes (4.3%) due to endophthalmitis[23,24] and 1 eye (2.1%) due to lost to follow-up.[28] In the group of eyes that failed due to the need for additional glaucoma surgery (n=13), 1 case underwent trab-trab[25], 3 trabeculectomy,[24] 1 ciclodestruction[28], 3 GDD[28] and 5 another type of surgery non-specified.[23]

C) Microcatheter assisted trabeculotomy – successful canalization

In this analysis of the 305 eyes that underwent MAT, in 197 eyes (64.6%) complete canalization of the Schlemm's canal with illuminated microcatheter was possible and in 108 eyes (35.4%) only partial canalization was undertaken. In 31 eyes (10.2%) MAT was not technically possible, therefore intraoperative conversion to CT was needed.

The comparative results between studies weren't homogeneous. Table 6 presents the comparison between complete and partial MAT. The analyses demonstrated that partial MAT had lesser success rates than complete MAT, with comparative information in this matter only in two studies. The first one with CS 82% and QS 82% vs CS 77% and QS 86%, respectively, at both 12 and 36 months follow-up. [21] The second one with CS 50% and QS 67% vs CS 96% and QS 100%, respectively, at 12 months follow-up.[7]

Six studies did not have information about the success rate between the 2 procedures [11,22-24,28,29] and the other three had information only about complete[25] or partial MAT.[26,27]

In two studies IOP reduction was higher with complete MAT vs partial MAT, with 60% vs 55%, respectively, in the first one[29] and 65% vs 52%, respectively, in the last one.[11]

No significant difference was achieved in these studies, neither in the success rates [7,11,21,23,24,26,29], in the postoperative IOP [11,24,26,29] or in the survival times[24].

In one study it was reported a higher need for medication in the partial MAT, p=0.180.[7]

D) Intraoperative Complications

Intraoperative complications of **MAT** were not uniformly reported by all studies. The most common complications were hyphema in 92 eyes (30.2%),[7,11,23,25] iris prolapse in 2 eyes (0.7%),[7,25] vitreous hemorrhage in 2 eyes (0.7%)[28] and catheter misdirection in 1 eye (0.3%).[22]

The only intraoperative complication with **conventional trabeculotomy** and **goniotomy** was hyphema and occurred in 66 eyes (21.6%) in the first one[23,25] and in 13 eyes (4.3%) in the second one.[11] The only intraoperative complication with **trab-trab** was iris prolapse in 30 eyes (9.8%).[7]

E) Postoperative Complications

E.1) Early Complications

Early postoperative complications with **MAT** included hyphema in 154 eyes (50.5%),[11,21,22,24,26,27-29] shallow AC in 6 eyes (2.0%),[23,24] vitreous hemorrhage in 2 eyes (0.7%),[28] transient hypotony with choroidal effusion in 1 eye (0.3%),[28] recurrent scleral cyst in 1 eye (0.3%),[28] and localized peripheral Descemet scar in 1 eye (0.3%).[28.]

Early postoperative complications with **conventional trabeculotomy** were hyphema in 23 eyes (7.3%),[24,27] shallow AC in 9 eyes (3.0%),[21,23,24] choroidal detachment in 1 eye (0.3%).[27]

The only early postoperative complication with **goniotomy** was hyphema in 13 eyes (4.3%).[11]

In **trab-trab** the most common complications were hyphema in 16 eyes (5.2%)[7] and shallow AC in 2 eyes (0.7%)[7].

E.2) Late Complications

The only two reported late complications (12 to 24 months of follow-up) associated with **MAT** were cataract in 4 eyes (1.3%)[23,24] and late endophthalmitis in 2 eyes (0.7%). [23,24]
With **conventional trabeculotomy** late complications included cataract in 5 eyes (1.6%),[23] lens subluxation in 2 eyes (0.7%).[23] Combined **trab-trab** presents as late complication one case (0.3%) with subcapsular cataract.

V – DISCUSSION

This review has included the eleven studies in the current literature that analyzed the efficacy and safety of MAT for the treatment of pediatric glaucoma. Some of these studies have compared the results of MAT with: goniotomy[11], CT[21,23-25,27], or Trab-Trab[7], and the remaining where case series only with MAT.[22,26,28,29] These studies are very heterogeneous in concerns of study methodology, patient selection, exclusion criteria and study outcomes. This heterogeneity precludes a proper statistical comparison.

From the 11 studies analyzed, 8 were case series[11,21-23,2-29,] and 3 were RCT.[7,24,25] According to the pyramid of scientific evidence[45], case series have the least validity of all types of clinical investigation, this being due to the great bias inherent to their study design, and so, quality of evidence tends to be poor. Such biases include selection bias by non-randomizing the sample leading to it possibly not being representative of the population, confirmation bias due to the same physician evaluating their own surgical results and information bias due to low follow up, possible errors in clinical records, no control group and unaccounted confounding factors. According to the above, 8 studies showed the typical limitations of retrospective case series, a low sample size and a short follow-up and the other 3 studies, as RCT, had the best scientific strength.

Although heterogenous, these studies have common grounds for comparison including: (1) most reported success rates were at 12 months of follow-up, (2) the mean preoperative IOP and number of medications was also similar between studies, (3) the success criteria were similar in most studies, which included achieving an IOP under a target value (1 study target IOP was ≤22 mmHg,[28] 4 studies <21 mmHg,[11,26,27,29] 3 studies ≤18 mmHg[22-24], one study ≤15mmHg[7] and another ≤12mmHg[25]), (4) need for additional surgery as a failure cause, that was reported in 6 of the 11 studies[23-26, 28] and (5) hyphema was reported as the most common intra and early postoperative complication in most studies.[7,11,21,22,23,25-27,29]

A) Illuminated microcatheter assisted trabeculotomy – Surgical success

Based on this review of literature, illuminated microcatheter–assisted circumferential trabeculotomy presented excellent success rates in most studies. As expected, surgical efficacy decreased over time with or without medications. The average complete success rate was 75.0% (33-87) at 12 months[11,21-29] and 65.5% (53-80) at 24 months[21,23,24,28] and the average qualified success rate was 86.8% (44-100) at 12 months[11,21-29] and 83.9% (76-90) at 24 months.[21,23,24,28] In most cases, good IOP control was achieved with a reduction of the number of glaucoma medications. At 12 months of follow-up the average IOP was 13.7±3.5mmHg (9-21)[7,11, 22-27] with 0.4±0.6 (0-1) medications.[11,22,23,26,27]

B) Glaucoma type The results achieved by this review seem to suggest that therapeutic interventions for SCG are both less successful and more likely to have technical difficulties (partial MAT or conversion to CT) in comparison to patients with PCG. At 12 months of follow-up, studies that only included PCG patients disclosed a mean CS of 78.9% and QS of 87.9% and studies that included SCG a CS of 57.8% and a QS of 64.4%.[11,21-29] Although the group of secondary glaucoma in children is very heterogenous, these results are possibly explained by the fact in this group there might be more angle dysgenesis and glaucoma may have a more aggressive prognosis.[29]

C) Previous glaucoma surgery When selecting patients for MAT, medical history also warrants attention as patients that underwent previous surgery (non-naïve) have lower success rates than naïve eyes. In this review, around 40% of the eyes that underwent MAT had a history of previous failed glaucoma surgery[11,21-23,26,29] and some of them had more than one procedure. Some studies performed a sub analysis comparing success rates between naïve and non- naïve eyes.[22,23,26,29] At 12 months of follow-up qualified success rate in naïve eyes ranged between 87.5-100%.[22,26,29] On the other hand, non-naïve eyes presented lower success rates, ranging from 44.4%-90.1%.[11,22,36,29]

Moreover, in the study from *Hu et al*[21] that only included PCG subjects (n=74) with previous failed glaucoma surgery, MAT was successfully performed in around two thirds of the cases (67.6%), with excellent success rate at 12 (84%) and 36 months (80%). Increased difficulty in performing MAT was likely related to SC damage and restriction of catheter passage because of the greater number of prior failed glaucoma surgeries.

Therefore, one can expect that not only cannulation of the SC might be more difficult in eyes that have previously undergone glaucoma surgery, but also the rate of success will be slightly lower. Although this surgical technique still proved to be an effective option for the management of complicated patients who had previously failed surgeries.

D) Complete vs Partial MAT The debate regarding the minimum degree of angle opening required for successful IOP reduction in pediatric glaucoma patients is controversial. In this review, some studies performed a sub analysis comparting the results between eyes with complete (>250º) and partial (180-250º) MAT.[11,21-29] Seven studies found no statistically difference in success rates between complete and partial MAT. [7,11,21,23,24,26,29] Nevertheless, there was a tendency for lower success rates in the eyes with partial MAT [7,21] and a higher need for medication.[7] Furthermore, there was higher IOP reduction with complete MAT.[11,29] However, no significant difference was achieved in the postoperative IOP [11,24,26,29] or in the survival times[24].

A major advantage of MAT, even when done partially, is that the illuminated tip facilitates the placement and advancement of the microcatheter. This allows for more accurate placement of the catheter for a precise opening of the inner wall of SC. It has been reported that aqueous humor outflow is segmental and that only two aqueous veins could account for all of aqueous outflow in normal human eye at any given time. Therefore, it makes sense that partial opening of Schlemm's canal may be sufficient to lower IOP so long as it is performed accurately.

E) Complications and Failure From this review hyphema was shown to be the most common intra (30.2%, n=92) and postoperative (40.5%, n=154) complication following MAT. This might be related to the greater extent of tissue disturbance with circumferential treatment, in comparison to conventional angle procedures which usually only treat 180º. On the other hand, as a greater extent of the angle is incised, one would might expect that the rate of shallow AC and choroidal detachment would be greater with this technique, however this was not observed. The rate of shallow AC with MAT was 2.0%, which was similar to the rate in CT (3.0%), and both were higher in comparison to goniotomy (0.7%). Moreover, choroidal detachment was rarely seen occurring only in 0.3% of the cases in MAT and CT, and it was not reported with goniotomy. When using the illuminated microcatheter, intraoperatively catheter misdirection occurred only in 1 eye (0.3%)[22] and there were no cases reported of Descemet trauma, irido or cyclodyalisis. Although, these studies did not report the rate of these complications when using the trabeculotome, from previous studies, rigid probe misdirection is known to be a major problem.[46] In the last years, several attempts have been made to minimize this problem including the use of prolene suture and now the illuminated microcatheter.[46]

There were also few late complications, after 12 to 24 months of follow-up, including cataract which occurred in 1.3%[23,24] and endophthalmitis in 0.7%,[23,24] with similar rates reported for CT (cataract 1.6% and endophthalmitis 0.7%).[23] Based on these results MAT seems to be a safe procedure with few sight threatening complications.

Regarding the causes for failure in eyes that underwent MAR, the 2 most common were the need for additional glaucoma surgery (41.3%)[22-26,28] and poor IOP control (28.3%).[7,21,23,28] In a minority (4.3%) failure was due to endophthalmitis[23,24] and there were no cases of failure due to loss of light perception. These results also support that trabeculotomy assisted my illuminated microcatheter discloses a good safety profile as a recent surgical procedure.

F) Comparison between MAT and other Pediatric Glaucoma Surgeries

F1) MAT vs CT There were four studies that compared the efficacy of 360º MAT over CT, three of these performed the classic 180º CT, [24,25,27] and one a two site 360º CT.[23] The results of the studies that compared MAT with 180º CT, confirmed the superiority of MAT in terms of higher IOP reduction as well as higher success rates.[24,25,27] Although patient selection was different between studies, as *Shakrawal et al.*[25] and *El Sayed et al.*[24] only included PCG patients, however *Shi et al.*[27] included different childhood glaucoma types (but mostly PCG). Additionally, these three studies excluded patients with previous glaucoma surgery, which allows a better comparison between results. Overall, at 12 months of follow-up the qualified success rate of MAT varied between 86.4%[27] and 90%[25], and at 24 months was 85.2% in *El Sayed et al.*[24] study. On the other hand, during the same follow-up period, CT qualified success rate in these studies ranged between 50-70%.[24,25,27]

The study by *El Sayed et al.*[23] disclosed different results, as two-site CT had a higher qualified success rate at final follow-up (mean 20months), CT 86.2% vs MAT 75.8%.

These results confirm that the microcatheter approach offers the advantage of in one passage incising the SC 360º, which has a higher success rate compared to 180º CT. [24,25,27] Additionally, with MAT as the microcatheter passes circumferentially over 360◦ and reappears from the opposite end of SC one can be sure that the whole canal was incised. Whereas CT is a relatively more blind procedure, and although it is preferred to deroof the SC underneath the scleral flap to make sure that the probe enters in the correct plane, one cannot guarantee that the probe will not become misdirected when it proceeds further circumferentially.

In comparison to the 2 site CT[23] the microcatheter technique failed to achieve superiority, nevertheless it presents one advantage being that only one scleral wound is performed hence allowing for a smaller area of conjunctival dissection. These authors state that, both techniques may be recommended as a first line procedure in pediatric eyes requiring trabeculotomy, however the added cost of the microcatheter could be an unnecessary financial burden in many places where pediatric glaucoma is common. Nevertheless, 2 site CT is a technique that most surgeons are not used to perform, as there is more experience with the classic 180º CT.[32,46]

Moreover, the study by *Hu et al.*[21] included PCG patients after previous failed glaucoma surgeries and analyzed the efficacy of MAT. One group included eyes with successful MAT (n=50) and the other group included eyes that intraoperatively MAT was not technically possible, and therefore converted to CT (n=24). After 12 months of follow up qualified success rate in MAT group was 80% and in the CT group was 55.8%. At 36 months MAT success rate maintained the same, however CT decreased to 37.0%. In this study, although MAT disclosed a higher success rate, it highlighted that in some cases where the passage of the illuminated microcatheter was interrupted by an obstruction and a completion of the trabeculotomy was attempted by the trabeculotome, the rigid probe managed to pass through the obstruction. It is likely that the flexibility and smaller diameter of the microcatheter makes it less resistant to obstructions in SC and more prone to become misdirected into the narrow collector channels.

F2) MAT vs Goniotomy Only one study compared the success rate of MAT with goniotomy in congenital glaucoma patients (most were PCG) and previous glaucoma surgery was not an exclusion criteria.[11] Similarly to the studies that compared MAT with CT, this study revealed that MAT had a statistically significant higher rate of success than goniotomy for CS (p=0.06) and QS (p=0.04). At 12 months of follow-up, qualified success with MAT was 91.6% exceeding the success rate of conventional goniotomy (QS 53.8%). The authors stressed that a possible significant bias between the two groups in this study was that more eyes in the MAT group had undergone previous surgery, which can lead to worse results in this group. As with CT, goniotomy only treats 180º in each surgery, which in comparison to 360º MAT might be responsible for the lower success rate of this technique. Furthermore, goniotomy demands a relatively transparent cornea, whereas MAT can be performed even in patients with severe corneal edema. Although, goniotomy has the advantage of being an ab interno procedure, therefore leaving the conjunctiva untouched, which in the future does not compromise the success rate of other glaucoma procedures which depend on the conjunctiva status.[32]

F3) MAT vs Trab-Trab In this review, we found one study that compared the success rate of MAT with combined Trab-Trab with MMC in PCG patients that had no previous history of glaucoma surgery.[7] The results were similar after 12 months of follow-up, CS was 86.7% and QS was 93.3% on the MAT group against a CS of 90.0% and QS of 93.3% on the Trab-Trab group. As the combined procedure is associated with a high rate of long-term complications, due to the presence of a bleb and the use of MMC, the authors suggest that MAT could be resorted to first, saving Trab-Trab for future intervention. However, the cost associated with the disposable illuminated microcatheter, steeper learning curve in comparison to conventional surgeries, and a higher incidence of hyphema were some of the disadvantages pointed out for the illuminated microcatheter trabeculotomy, factors that may hold special relevance in developing nations.

Finally, another main advantage of MAT worth noting is the ability to treat the entire angle in one surgery, which minimize anesthetic risks. Retrospective studies in humans have shown a higher prevalence of learning disabilities in children who received multiple exposures to general anesthesia before the age of 4 years. Animal studies suggest an association between general anesthesia and neurodevelopmental delay. Therefore, the relative lifelong risks and complications of general anesthetic exposure should be considered when recommending surgery, especially in light of the child's age, health status and necessity of multiple anesthetic events.[49]

VI - CONCLUSIONS

Pediatric glaucoma surgery is challenging in many aspects, from appropriate surgical planning and intraoperative technique to postoperative management. For PCG patients who present before 1 year of age, goniotomy and trabeculotomy have good success rates. However, in patients with pediatric glaucoma with a poor prognosis, such as aphakic glaucoma or secondary glaucoma associated with ocular or systemic anomalies, the success rates are lower. Furthermore, approximately 20% of angle surgeries fail over time and a second procedure will be required. CT seems to be more effective than either procedure alone in more severe cases of congenital glaucoma. Filtration surgery, in the form of trabeculectomy or combined Trab-trab and GDD surgery, may be necessary when maximal medical therapy fails.

This literature review showed that illuminated microcatheter assisted circumferential trabeculotomy can be successfully used to catheterize Schlemm's canal and perform partial and full circumferential trabeculotomy for the treatment of pediatric glaucoma. It seems to provide excellent pressure-lowering effect with minimal complications in the early postoperative course (up to 24 months). Even in patients with previous surgeries, the effect was comparable to that in eyes that underwent this procedure as an initial intervention.

Based on this analysis, illuminated microcatheter–assisted trabeculotomy offers few advantages over other conventional surgeries. There is minimal risk of false passage creation with guided endo-illuminator passage, unlike the Harms or suture trabeculotomy. Moreover, the incidence of adverse effects associated with full thickness trabeculectomy, such as shallow anterior chamber, cataract formation, infections, late hypotony, and suprachoroidal hemorrhage were lower with MAT. Also, postoperative inflammation could be lesser with MAT owing to the minimal iris manipulation required. However, the cost associated with the disposable illuminated microcatheter and steeper learning curve in comparison to conventional surgeries are some of the disadvantages of illuminated microcatheter trabeculotomy that may hold special relevance in developing nations and could be an unnecessary financial burden in many places where pediatric glaucoma is common.

In the future, further research is warranted to determine the long-term success and safety of this procedure.

VII - ACKNOWLEDGEMENTS

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IX – ANNEXES

IX.I – FIGURES

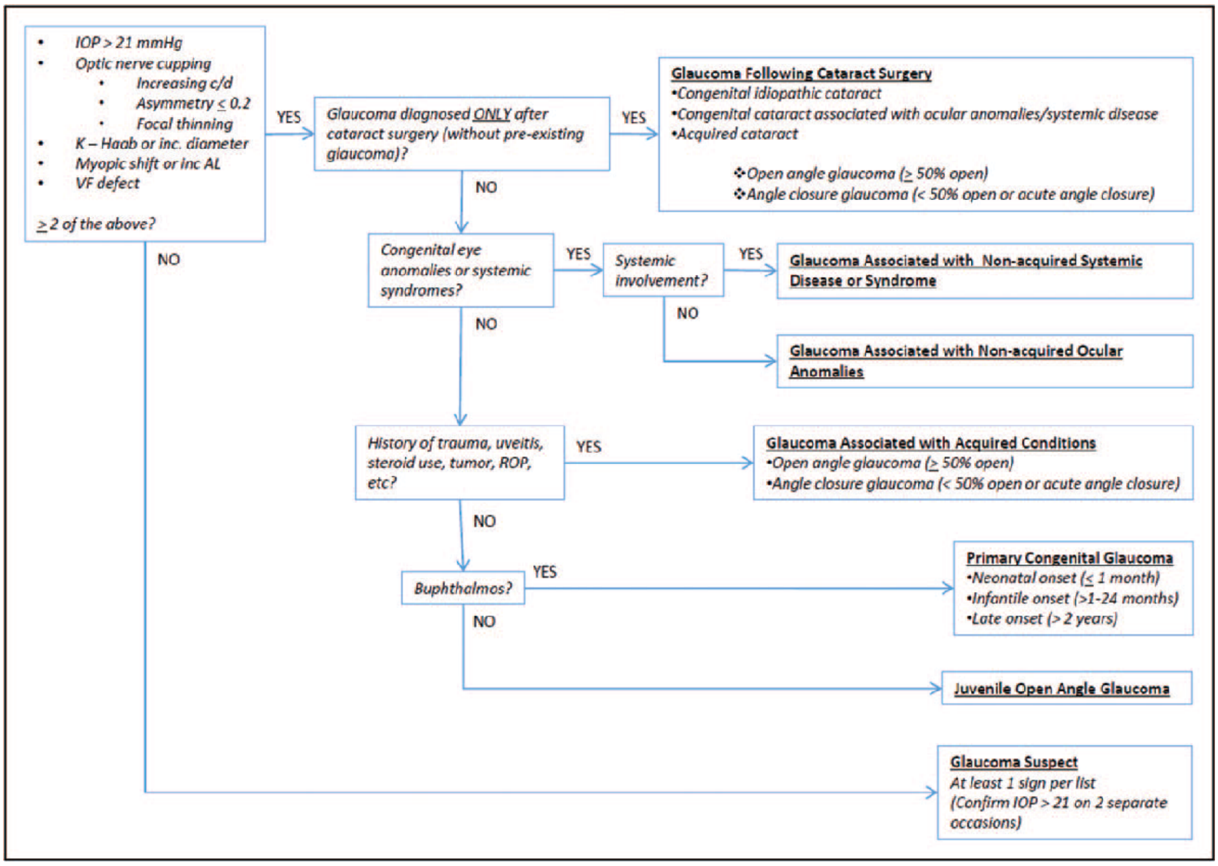

Figure 1. Diagnostic criteria and Classification system for pediatric glaucoma. *Adapted from New classification system for pediatric glaucoma: implications for clinical care and a research registry.* [30]

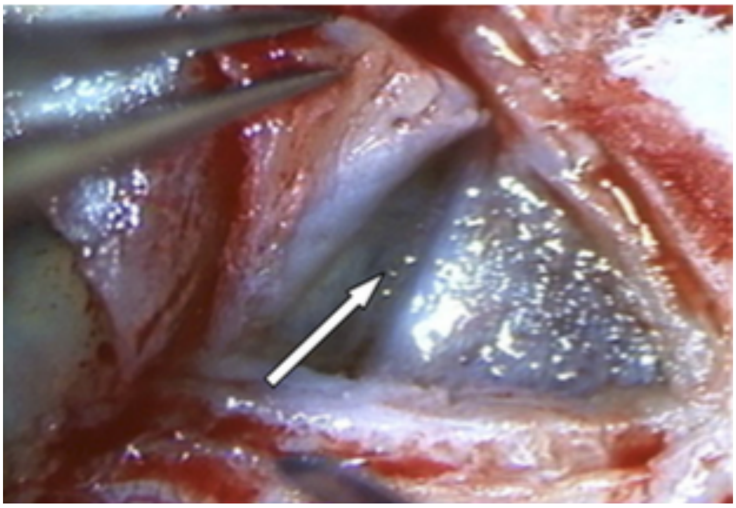

Figure 2. Exposure of Schlemm's canal (arrow). *Adapted from Canaloplasty for Adult OAG Interim Clinical Study Analysis* [12]

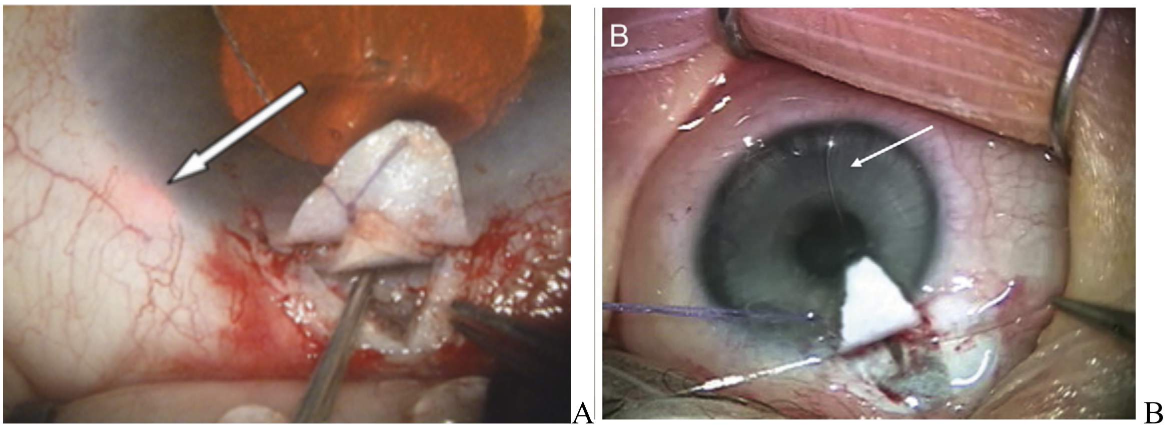

Figure 3. Ab externo Trabeculotomy assisted with illuminated microcatheter. A - Catheterization of Schlemm's canal with beacon tip visible through sclera (arrow). B - Trabecular tensioning sutures (arrow) in Schlemm's canal. Two suture loops are in place. *Adapted from Canaloplasty: Circumferential viscodilation and tensioning of Schlemm's canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults.* [12]

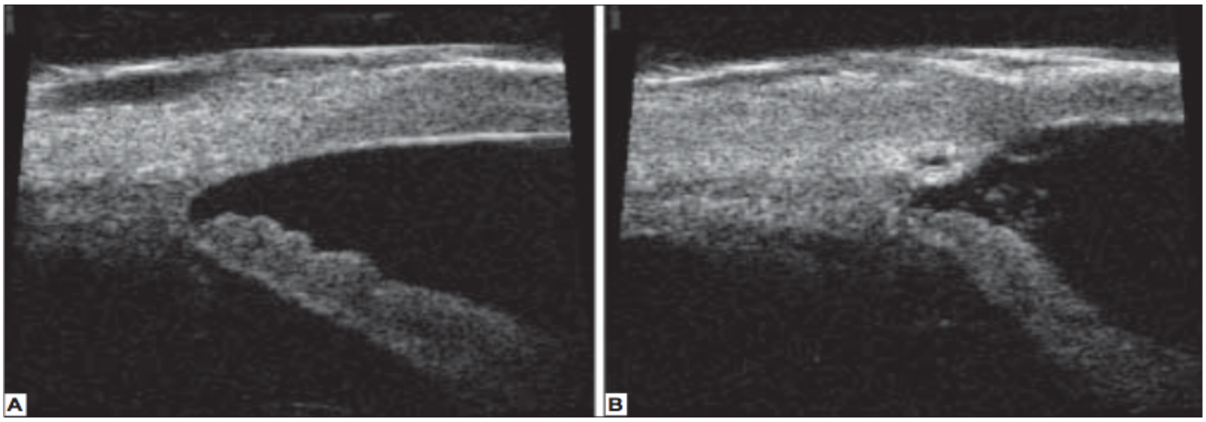

Figure 4. The UBM images of the anterior angle before (left) and after (right) canaloplasty showing dilation of Schlemm's canal. The tensioning suture is noted by the arrow. *Adapted from Canaloplasty: Circumferential viscodilation and tensioning of Schlemm's canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults.*[12]

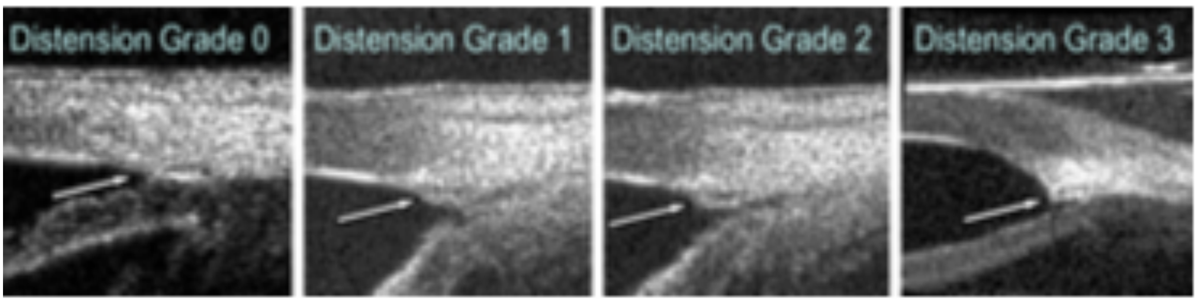

Figure 5. The UBM images of exemplary trabecular meshwork dis- tension grades. Arrows indicate the location of tissue distension. *Adapted from Canaloplasty: Circumferential viscodilation and tensioning of Schlemm's canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults.*[12]

Figure 6. The iTrack microcatheter used has a 200µm diameter shaft with a blunt distal tip of about 250 µm in diameter. *Adapted from Canaloplasty: Circumferential viscodilation and tensioning of Schlemm's canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults.*[12]

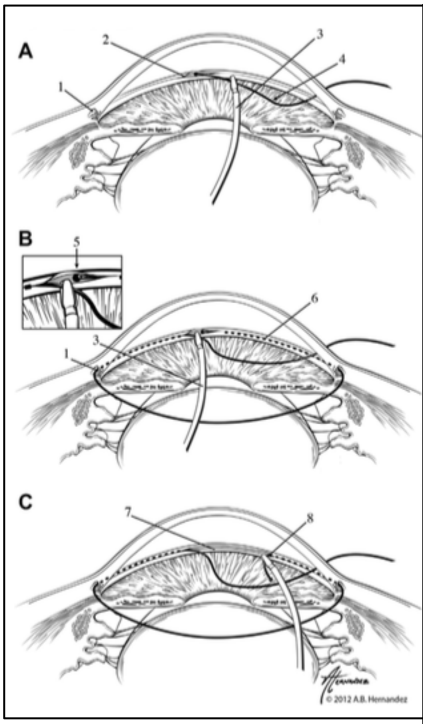

Figure 7. Gonioscopy-assisted ab-interno 360º trabeculotomy procedure with suture. A - Initial cannulation of Schlemm's canal (SC) within the AC. B - The catheter (or suture) is passed 360º around the canal. C - The distal tip of the catheter (or suture) is retrieved and externalized, creating circumferential trabeculotomy.

(1) SC; (2) Initial goniotomy site; (3) Microsurgical forceps; (4) Either the suture or microcatheter; (5) Distal end of the suture or microcatheter after it passing 360º around SC; (6) Path of the suture or microcatheter within SC; (7) Trabecular shelf that is created after this procedure; (8) Trabeculotomy that is created when the distal end of the suture or catheter is retrieved and externalized.

Adapted from Gonioscopy-Assisted Transluminal Trabeculotomy, Ab Interno Trabeculotomy Technique Report and Preliminary Results [14]

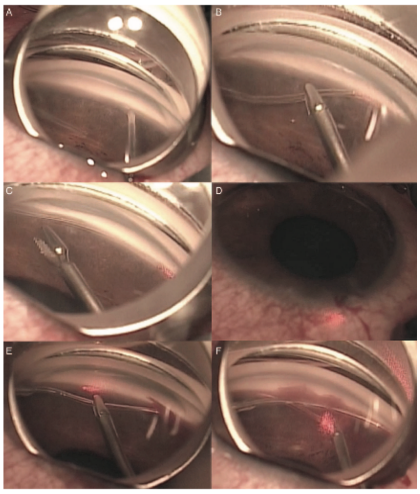

Figure 8. Gonioscopy-assisted ab interno trabeculotomy with illuminated microcatheter. (A) Initially a goniotomy is created with an MVR blade. (B) Schlemm's canal (SC) is then cannulated with a microcatheter, using microsurgical forceps. (C) The catheter was passed 2–3 clock hours around SC. (D) The catheter has passed 180° around the canal. (E) The microcatheter has come full circle around the canal. (F) The distal tip of the catheter is retrieved within the AC using microsurgical forceps.

Adapted from Gonioscopy assisted transluminal trabeculotomy: An ab interno circumferential trabeculotomy for the treatment of primary congenital glaucoma and juvenile open angle glaucoma. [3]

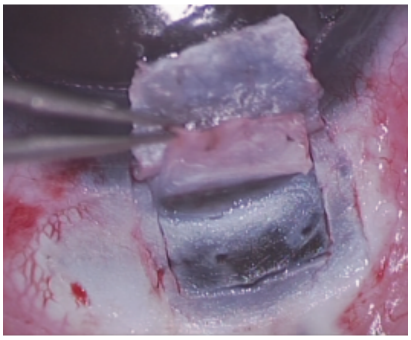

Figure 9. Deep sclerectomy performed in a child with glaucoma secondary to Sturge-Weber Syndrome. *Adapted from Current Surgical Options for the Management of Pediatric Glaucoma* [6]

IX.II – Tables

	Goniotomy	Trabeculotomy (probe)	Trabeculotomy (360°) Suture	Trabeculotomy (360°) Illuminated microcatheter	Trabeculotomy-Trabeculectomy
Conjunctival incision	−	+	+	+	+
Possible with opaque cornea (angle structures not clearly visible)	−	+	+	+	+
Angle visualisation	+	−	− (only with gonio lens)	+	−
Specialised instruments/skills	+ +	+	+	+ +	+ +
Extent of surgical trauma	+	+ +	+ +	+ +	+ + +
Safety	+ +	+	+	+ +	+
Duration of surgery	+	+ +	+ + to + + +	+ + to + + +	+ +
Can be repeated	+ +	+ +	−	−	+
Bleb-related complications	−	− / +	− / +	− / +	+

Table 1. Comparison of Angle Surgery Techniques for Pediatric Glaucoma. *Adapted from Childhood glaucoma in the 21st century.*[1]

Title	Country Year	Aims Success criteria	Surgical groups	Inclusion criteria	Exclusion criteria	Success rate	Failure causes
Hu et al.[21]	China 2019	**Aim:** Evaluate effectiveness of MAT to treat PCG after failed previous glaucoma surgeries. **Success criteria*:** Final IOP ≤21 mmHg with (QS) or without (CS) medications.	**Group 1:** MAT – 50 eyes. **Complete MAT (≥330º)** - 22 eyes. **Partial MAT (180º-330º)** - 28 eyes. **Group 2:** Cases converted to CT, when SC couldn't be catheterized >180º - 24 eyes.	• The previous failed glaucoma surgeries (≥1 CT or filtering surgery). • Diagnosis of PCG: (1) isolated trabeculodysgenesis (2) No other ocular/ systemic abnormality. (3) Elevated IOP, increased corneal diameter, corneal edema, increased axial length, and glaucomatous optic nerve cupping.	• Previous ophthalmic surgery other than glaucoma surgery; • > 180º of PAS.	**Group 1:** QS 84.0%, and CS 80.0% at both 12 and 36 months postoperative. **Complete MAT:** QS and CS 86.4% at 12 months; QS and CS 77.3% at 36 months post-operative. **Partial MAT:** QS and CS 82.2% at 12 and 36 months post-operative. **Group 2:** QS 55.8%, and CS 33.3% at 12 months and QS 37.0% and CS 29.2% at 36 months post-operative.	**Group 1:** 4 eyes – uncontrolled IOP. Eyes with failure had a significantly higher number of previous surgeries p<0.001 **Group 2:** No info.
Toschev et al.[22]	Germany 2018	**Aim:** Determine feasibility, efficacy, and safety of MAT for congenital glaucoma. **Success criteria*:** Final IOP ≤18 mm Hg with (QS) or without (CS) medications.	**Group 1:** PCG naïve (**)– 23 eyes. **Group 2:** PCG non-naïve (**) - 3 eyes; SCG - 10 eyes (4 of them non-naïve).	• Childhood glaucoma; • Non-naïve eyes were not excluded.	No info.	**Group 1:** CS 80.0%, QS 100.0%, at 14 months. **Group 2:** CS 33.3%, QS 44.4% at 8 months. *	**Group 1:** no failures. **Group 2**: 5 eyes failed – SC occlusion or high tissue resistance of TM, all converted to CT.
El Sayed et al.[23]	Egypt 2018	**Aim:** Compare the outcomes of MAT with 2 site CT (360º) in PCG patients. **Success criteria*:** Final IOP ≤18 mm Hg with (QS) or without (CS) medications.	**Group 1**: MAT – 33 eyes. Previous goniotomy 18.2%. **Group 2:** CT – 59 eyes. Previous goniotomy 16.9%.	• PCG; • Age < 12 years-old; • ≥ 6 months follow-up; • Eyes with previous goniotomy were not excluded.	• Combined procedures; • Previous CT; • CT ≤ 270º; • MAT <180º.	At final follow-up (mean 19.7 months): **Group 1**: MAT 72.7% CS and 75.8% QS; 58% complete 360◦ incision; **Group 2:** CT 81.0% CS and 86.2% QS; 56% had complete 360º incision; Mean survival time MAT - 20.9±1.3 months and CT 21.4±0.92 months.	No significant difference in failure rates between groups p=0.200 **Group 1:** 8 eyes– 5 need another glaucoma surgery, 2 elevated IOP and 1 late post-operative endophthalmitis. **Group 2:** 8 eyes – 7 need another glaucoma surgery and 1 uncontrolled IOP.
El Sayed et al.[24]	Egypt 2017	**Aim:** Compare the outcomes of MAT to CT in childhood glaucomas. **Success criteria*:** Final IOP ≤18 mm Hg with (QS) or without (CS) medications.	**Group 1:** MAT – 30 eyes Complete (360º) - 50% Partial (250-250º) - 50% **Group 2:** CT – 32 eyes	• PCG; • Age < 10 years old; • ≥6 months follow-up; • In bilateral cases, only 1 eye was included (higher IOP).	• Previous surgery; • Combined procedures; • Trabeculotomy involved ≤120° SC.	At 2 years of follow-up: **Group 1:** MAT – CS 66.7% and QS 85.2% 3 lost of follow-up. **Group 2:** CT – CS 46.7% and QS 50.0% 2 lost of follow-up. The mean survival time was significantly longer (p=0.01) for MAT (19.3±1.6 months) compared to CT (12.4±1.8 months).	**Group 1:** 4 eyes– 3 need for another glaucoma surgery; 1 late endophthalmitis. **Group 2:** 16 eyes– 13 need for additional glaucoma surgery and 3 no motif was reported.

***Shakrawal et al.*[25]**	India 2017	**Aim:** Compare 1-year outcomes of MAT vs CT in PCG. **Success criteria*:** Final IOP ≤12mmHg with (QS) or without (CS) medications.	**Group 1:** MAT – 20 eyes Complete 80%. **Group 2:** CT – 20 eyes.	• PCG unilateral or bilateral; • Age <2 years old.	• Secondary glaucoma; • Previous eye surgery; • Parents not willing for consent and follow-up.	At 12 months of follow-up: **Group 1:** CS 80%, QS 90%; **Complete MAT:** CS 87.5%; QS 93.8%; **Group 2:** CS 60%, QS 70%. Differences in success rates (CS and QS) between groups were statistically significant (p< 0.001).	**Group 1:** 4 eyes – 1 need for additional glaucoma surgery and 3 no motif was reported. **Group 2:** 6 eyes – 4 need for additional glaucoma surgery and 2 no motif was reported.
***Shi et al.*[26]**	China 2017	**Aim:** Compare surgical outcomes of MAT following failed angle surgeries with the ones with no previous angle surgery, in PCG. **Success criteria*:** Final IOP ≤21 mmHg and 30% reduction with (QS) or without (CS) medications.	**Group 1:** Patients without previous angle surgeries – 20 eyes. **Group 2:** Patients who underwent ≤ 2 previous failed angle surgeries (goniotomy, trabeculotomy, trab-trab) – 22 eyes.	• Diagnosis of PCG: (1) isolated trabeculodysgenesis (2) No other ocular/ systemic abnormality. (3) Elevated IOP, increased corneal diameter, corneal edema, increased axial length, and glaucomatous optic nerve cupping.	• Previous > 2 angle surgeries; • Previous ophthalmic surgery besides angle surgeries; • >180° of PAS.	At 12-month follow-up: **Group 1:** CS 78.9%, QS 90.0%; **Group 2:** CS and QS 77.3%. No statistical significant difference between groups (CS p=0.85; QS p=0.29).	**Group 1:** 2 eyes, no motives reported. **Group 2:** 2 eyes – 1 need for additional glaucoma surgery and 1 no motif reported.
***Shi et al.*[27]**	China 2016	**Aim:** Compare the outcomes of MAT to CT in childhood glaucomas. **Success criteria*:** Final IOP ≤ 21 mm Hg and 30% reduction with (QS) or without (CS) medications.	**Group 1:** MAT – 22 eyes. **Group 2:** CT – 21 eyes.	• Diagnosis of childhood glaucoma including elevated IOP, increased corneal diameter, corneal edema, increased axial length and glaucomatous cupping of the optic nerve; • Examination under anesthesia with 80MHz UBM to access suitability for trabeculotomy.	• Previous surgery; • >180° of PAS.	At 12-month follow-up: **Group 1:** CS 81.0% and QS 86.4%. **Partial MAT**: (n=3) all eyes were successful at 12-month follow-up. **Group 2:** CS 51.6% and QS 61.9%. No statistical significant difference between groups for QS (p=0.06), however for CS significance was found (p=0.04).	**Group 1:** 3 eyes, no motives reported. **Group 2:** 9 eyes – 4 need for additional glaucoma surgery and 5 no motives reported.
***Temkar et al.*[7]**	India 2015	**Aim:** To compare outcomes of MAT vs combined Trab-Trab with MMC for PCG. **Success criteria*:** Final IOP ≤15mmHg with (QS) or without (CS) medications.	**Group 1**: MAT – 30 eyes. **Group 2:** Trab-Trab MMC – 30 eyes.	• Bilateral PCG; • age < 2 years-old; • Examination under anesthesia to confirm the disease and its baseline severity.	• Unilateral disease; • secondary glaucoma; • previous ocular surgery; • parents not willing for consent and follow-up.	At 12 months of follow-up: **Groups 1:** CS 86.7%; QS 93.3%; **Group 2:** CS 90.0%; QS 93.3%. No statistical significant difference between groups for QS (p=1.00) or CS (p>0.99).	**Group 1:** 2 eyes, uncontrolled IOP. **Group 2:** 2 eyes, uncontrolled IOP.

Dao et al.[28]	USA 2014	**Aim:** To determine the safety and efficacy of MAT for refractory aphakic glaucoma and JOAG. **Success criteria*:** Final IOP ≤22mmHg and > 30% reduction, and glaucoma stability with or without medications.	**Group 1:** Aphakic glaucoma – 13 eyes; **Group 2:** JOAG – 10 eyes.	• ≥6 months follow-up; • JOAG < 30 years at time of diagnosis; • In bilateral cases, only the 1st operated eye was included.	• Anterior segment anomalies; • Extensive PAS; • Congenital glaucoma; • Previous/planned ocular surgery (other than secondary IOL).	At 24-month follow-up: **Group 1:** CS 0.0% and QS 61.5%; **Group 2:** CS 20.0% and QS 90.0%.	**Group 1:** 5 eyes – 3 need of additional surgery, 1 uncontrolled IOP; 1 lost of follow-up. **Group 2:** 1 eye, need of additional surgery.
Girkin et al.[29]	USA 2012	**Aim:** To determine the safety and efficacy of MAT for congenital glaucoma. **Success criteria*:** Final IOP <21 mmHg and > 30% reduction with (QS) or without (CS) medications.	**Total:** 11 eyes.	• Diagnosis of childhood glaucoma including elevated IOP, increased corneal diameter, corneal edema, increased axial length and glaucomatous cupping of the optic nerve; • ≥6 months follow-up • Eyes with previous angle surgery were not excluded.	No info.	At 12 months of follow-up: • CS 81.8% and QS 90.1%; • If eyes with previous angle surgery were excluded, CS 87.5% and QS 100%.	1 eye, no motif reported.
Girkin et al.[11]	USA 2012	**Aim:** To compare MAT with goniotomy for congenital glaucoma. **Success criteria*:** Final IOP <21 mmHg and > 30% reduction with (QS) or without (CS) medications.	**Group 1:** MAT – 11 eyes; 6 eyes 360º, 3eyes 370º, 2eyes 180º. **Group 2:** Goniotomy – 13 eyes.	• Diagnosis of childhood glaucoma including elevated IOP, increased corneal diameter, corneal edema, increased axial length and glaucomatous cupping of the optic nerve.	No info.	At 12 months follow-up: **Group 1:** MAT – QS 91.6% and CS 83.3%; **Group 2**: Goniotomy QS 53.8% and CS 46.2%. Difference between groups was statistically significance. The survival curves show that MAT had a higher rate of success than goniotomy for CS (p=0.06) and QS (p=0.04).	**Group 1:** 1 eye, no motif reported. **Group 2:** 6 eyes, no motif reported.

Table 2. Ten studies comparison with illuminated microcatheter assisted trabeculotomy – Study's aims, success criteria, inclusion and exclusion criteria, success rate and failures.

Abbreviations: AC: anterior chamber; CS: complete success; CT: Conventional Trabeculotomy; IOL- intraocular lens; IOP: intraocular pressure; JOAG: juvenile open angle glaucoma; MAT- microcatheter assisted trabeculotomy; MMC- mitomycin C; QS: qualified success; PAS: peripheral anterior synechiae; PCG: primary congenital glaucoma; SC-schlemm's canal; TM: trabecular meshwork; Trab-Trab: trabeculotomy-trabeculectomy; UBM: ultrasound biomicroscopy.

(*) failure was considered if no such pressure could be achieved despite maximum tolerated medical treatment, or if a subsequent glaucoma procedure was needed to control the IOP or if a devastating complication occurred (e.g. retinal detachment, endophthalmitis or supra-choroidal haemorrhage). (**) naïve eyes are eyes considered naïve to glaucoma surgeries and non-naïve eyes are eyes that already underwent previous glaucoma surgeries.

Title	Mean IOP (range), mmHg				Mean number of glaucoma medications (range)				Surgical Complications		
	Preoperative	**6M*****	**12M*****	**At final follow-up**	**Preoperative**	**6M*****	**12M*****	**At final follow-up**	**Intraoperative**	**Early Postoperative**	**Late Postoperative**
Hu et al.[21]	**Group 1 -** 35.3±7.0 **Group 2 -** 33.1±6.3	No info.	No info.	**At 3 years Group 1 -** 17.7±8.6 p<0.001** **Group 2 -** 25.8±10.0 p=0.004**	**Group 1 -** 2.7±0.8 **Group 2 -** 3.0±0.7	No info.	No info.	**At 3 years Group 1 -** 0.6±1.2, p<0.001** **Group 2 -** 2.0±1.4, p=0.002**	Hyphema (*n not reported*).	**Group 1 –** 1 eye transient hyphema. **Group 2 -** 1 eye transient shallow AC.	No info.
Toschev et al.[22]	**Group 1 -** 28.6±5 **Group 2 -** 29.6±9	No info.	**Group 1 -** 13±2.7 **Group 2 -** 20.2±7.1	No info.	**Group 1 -** 0.8 **Group 2 -** 1.8	No info.	**Group 1 -** 0.3 **Group 2 -** 0.9	No info.	1 eye catheter misdirection (had previously history of CT).	All eyes had mild hyphema.	No info.
El Sayed et al.[23]	**Group 1 -** 24.0±5.9 (12-38) **Group 2 -** 23.3±5.0 (14-35) p=0.530*	**Group 1**11.9±4.3 (8-28) **Group 2**12.4±4.1 (6-32) p=0.560*	**Group 1 -** 12.6±4.1 (7-24) **Group 2 -** 12.2±3.0 (6-22) p=0.640*	**At 3 years: Group 1 -** 13.3 ± 5.0 (6-28) **Group 2 -** 13.6 ± 4.8 (6-32) p=0.820*	**Group 1 -** 0.8 ± 1.0 (0-3) **Group 2 -**1.5 ± 0.8 (0-3) p<0.050*	**Group 1 -** 0.3±0.7 (0-2) **Group 2 -** 0.2±0.5 (0-2) p=0.120*	**Group 1 -** 0.3±0.7 (0-2) **Group 2 -** 0.1±0.3 (0-1) p=0.020*	**At 3 years: Group 1 -** 0.5±0.9 (0-3) **Group 2 -** 0.3±0.7 (0-3) p=0.310*	All eyes hyphema.	**Group 1 -** 3 eyes transient shallow AC. **Group 2 -** 7 eyes transient shallow AC.	**Group 1 -** 1 eye endophthalmitis at 13 m and 3 eyes cataract. **Group 2 -** 5 eyes cataract and 2 eyes lens subluxation (90-180º).
El Sayed et al.[24]	**Group 1 -** 25.1±6.4 (12-38) **Group 2 -** 22.3±5.2 (14-32) p=0.090*	**Group 1 -** 11.8±4.4 (6-28) **Group 2 -** 12.6±4.4 p=0.040*	**Group 1 -** 11.9±3.4 (7-24) **Group 2 -** 12.8±4.4 (8-22) p=0.500*	**At 2 years: Group 1 -** 11.4±2.5 (8-16) **Group 2 -** 12 .6±4.4 (8-24) p=0.400*	**Group 1 -** 0.6±0.9 (0-3) **Group 2 -** 0.6±1.0 (0-3) p=0.900*	**Group 1 -** 0.5±0.8 (0-2) **Group 2 -** 0.7±0.9 (0-3) p = 0.400*	**Group 1 -** 0.2±0.6 (0-2) **Group 2 -** 0.4±0.8 (0-2) p=0.500*	**At 2 years: Group 1 -** 0.2±0.5 (0-2) **Group 2 -** 0.3±0.8 (0-2) p=0.700*	No info.	**Group 1 -** 3 eyes transient shallow AC; and 2 eyes transient hyphema. **Group 2 -** 1 eye transient shallow AC and 2 transient eyes hyphema.	**Group 1 -** 1 eye endophthalmitis and 1 eye cataract. **Group 2 -** none.
Shakrawal et al.[25]	**Group 1 -** 24.7±3.9 **Group 2 -** 24.6±3.3	**Group 1**10.0±2.7 **Group 2**12.4±2.0 p<0.040*	**Group 1 -** 9.5±2.4 **Group 2 -** 11.7±2.1 p<0.000*	No info.	No info.	No info.	No info.	No info.	**Group 1 -** 1 eye iris prolapse and 18 eyes hyphema. **Group 2 -** 7 eyes hyphema.	None.	**No info.**
Shi et al.[26]	**Group 1 -** 31.5±7.2 **Group 2 -** 34.6±7.3	No info.	**Group 1 -** 15.6±3.1 **Group 2 -** 16.0±4.6 p<0.000*	No info.	**Group 1 -** 3 (0-5) **Group 2 -** 3 (1-4) p<0.001*	No info.	**Group 1 -** 0 (0-4) **Group 2 -** 0 (0-2) p<0.000*	No info.	Hyphema (*n not reported*).	All eyes transient hyphema.	No info.

***Shi et al.*[27]**	**Group 1 -** 33.1±6.1 **Group 2 -** 33.2±7.2 p=0.050*	**Group 1** 17.0±5.1 **Group 2** 22.5±9.8 p=0.040*	**Group 1 -** 14.8±2.5 **Group 2 -** 19.0±7.1 p<0.000*	No info.	**Group 1 -** 3 (1–5) **Group 2 -** 2 (1–4) p= 0.001*	**Group 1 -** 0.5 ± 1.1 **Group 2 -** 1.3 ± 1.5 p=0.020*	**Group 1 -** 0.1±0.3 (0-1) **Group 2 -** 1.3±1.5 (0-4) p=0.040*	No info.	Hyphema (*n not reported*).	**Group 1** - All eyes transient hyphema. **Group 2 -** 1 eye transient choroidal detachment.	No info.
***Temkar et al.*[7]**	**Group 1 -** 21.8±9.8 **Group 2 -** 21.7±8.9 p=0.840*	**Group 1** 11.4±2.2 **Group 2** 11.1±2.3 p=0.530*	**Group 1 -** 11.6±3.3 **Group 2 -** 11.6±3.0 p=0.960*	No info.	No info.	No info.	No info.	No info.	**Group 1 -** 1 eye iris prolapse, 30 eyes hyphema (2 total hyphema). **Group 2** - All eyes iris prolapse.	**Group 1** – 29 eyes transient hyphema; 1 hyphema needed drainage. **Group 2** - 16 eyes transient hyphema; 2 eyes transient shallow AC.	**Group 2 -** 1 eye subcapsular cataract.
***Dao et al.*[28]**	**Group 1 -** 35.4±4.7 **Group 2 -** 30.4±7.1	No info.	No info.	**At 47 m follow-up:** **Group 1 -** 21.9±8.6 p=0.0004** **Group 2 -** 14.4±4.3 p<0.0001**	**Group 1 -** 2.5 (2-4) **Group 2 -** 3.5	No info.	No info.	**At 47 m follow-up:** **Group 1 -** 1.9 p=0.070** **Group 2 -** 2.2 p=0.030**	**Group 1** - 2 eyes vitreous haemorrhage.	**Group 1 -** Transient hyphema common (*n not reported*); 1 eye transient choroidal effusion; 1 eye recurrent scleral cyst; 1 eye Descemet scar; 2 eyes vitreous haemorrhage (both requiring PPV). **Group 2 -** 2 eyes transient hyphema.	No info.
***Girkin et al.*[29]**	33.8±6.3	18.3±3.5 p<0.001)**	No info.	No info.	No info.	No info.	No info.	No info.	No info.	All eyes transient hyphema.	No info.
***Girkin et al.*[11]**	**Group 1 -** 35.7 **Group 2 -** 36.3 p=0.877*	No info.	No info.	**Group 1 -** 17.1±3.5 **Group 2 -** 25.3±11.9 p=0.031 *	**Group 1 -** 1.6±0.6. **Group 2 -** 1.6±0.7	No info.	No info.	**Group 1 -** 0.4±0.9 **Group 2 – 1.1**±1.1	All eyes hyphema.	All eyes transient hyphema.	No long-term complications in either group.

Table 3. Data regarding pre and postoperative: IOP, number of medications and surgical complications during follow-up time – ten studies comparison with illuminated microcatheter assisted trabeculotomy. *comparison between groups **comparison between preoperative and postoperative. ***IOP postoperative at 6 and 12 months.

Abbreviations: AC: anterior chamber; CT: conventional trabeculotomy; IOP: intraocular pressure; M: month; n: number.

Study	*Hu et al.*[21]		*El Sayed et al.*[23]	*El Sayed et al.*[24]	*Shi et al.*[26]		*Shi et al.*[27]	*Dao et al.*[28]		*Girkin et al.*[29]	*Girkin et al.*[11]
Patients, number	22	28	33	30	20	22	22	13	10	11	11
Study design	PCG after failed surgery		PCG MAT vs CT	Childhood glaucoma MAT vs CT	MAT in PCG after failed surgery		Childhood glaucoma MAT vs CT	MAT Aphakic	MAT JOAG	MAT Congenital glaucoma	Congenital glaucoma MAT vs goniotomy
	Complete MAT ≥330º	Partial MAT <330º			No previous	≤ 2 previous					
M1	-	-	100.0%	83.3%	85.0%	86.4%	95.5%	-	-	100.0%	100.0%
M3	-	-	72.7%	70.0%	85.0%	81.8%	90.9%	-	-	90.1%	100.0%
M6	-	-	69.7%	64.3%	85.0%	77.3%	90.9%	-	-	81.8%	83.3%
M12	86.4%	82.2%	72.7%	70.3%	78.9%	77.3%	81.0%	-	-	81.8%	83.3%
M24	-	-	72.7%	66.6%	-	-	-	0.0%	20.0%	-	-
M36	86.4%	82.2%	-	-	-	-	-	-	-	-	-

Table 4. Comparison between cumulative probability of **complete success** for microcatheter assisted trabeculotomy. Abbreviations: CT: conventional trabeculotomy; JOAG: juvenile open angle glaucoma; M: month; MAT: microcatheter assisted trabeculotomy; PCG: primary congenital glaucoma.

Abbreviations: CT: conventional trabeculotomy; JOAG: juvenile open angle glaucoma; M: month; MAT: microcatheter assisted trabeculotomy; PCG: primary congenital glaucoma.

Study	*Hu et al.*[21]		*El Sayed et al.*[23]	*El Sayed et al.*[24]	*Shi et al.*[26]		*Shi et al.*[27]	*Dao et al.*[28]		*Girkin et al.*[29]	*Girkin et al.*[11]
Patients, number	22	28	33	30	20	22	22	13	10	11	11
Study design	PCG after failed surgery		PCG MAT vs CT	Childhood glaucoma MAT vs CT	MAT in PCG after failed surgery		Childhood glaucoma MAT vs CT	MAT		MAT Congenital glaucoma	Congenital glaucoma MAT vs goniotomy
	complete MAT ≥330º	partial MAT <330º			No previous	≤ 2 previous		Aphakic	JOAG		
M1	-	-	100.0%	93.3%	90.0%	84.2	95.5%	76.9%	90.0%	100.0%	100-0%
M3	-	-	90.9%	93.3%	90.0%	90.9	90.9%	69.2%	90.0%	90.1%	100.0%
M6	-	-	87.9%	89.9%	90.0%	86.4	90.9%	61.5%	90.0%	90.1%	100.0%
M12	77.3%	82.2%	87.9%	89.9%	90.0%	77.3	86.4%	61.5%	90.0%	90.1%	91.6%
M24			75.8%	85.2%	-	-	-	61.5%	90.0%	-	-
M36	77.3%	82.2%	-	-	-	-	-	-	-	-	-

Table 5. Comparison between cumulative probability of **qualified success** rate for microcatheter assisted trabeculotomy. Abbreviations: CT: conventional trabeculotomy; JOAG: juvenile open angle glaucoma; M: month; MAT: microcatheter assisted trabeculotomy; PCG: primary congenital glaucoma.

Abbreviations: CT: conventional trabeculotomy; JOAG: juvenile open angle glaucoma; M: month; MAT: microcatheter assisted trabeculotomy; PCG: primary congenital glaucoma.

Article	Study design	Patients in the MAT group, number			Conversion CT	Success rate		Comparison
		Total	Complete	Partial		Complete MAT	Partial MAT	
Hu et al.[21]	PCG after failed surgery MAT complete vs. partial	50	22 All ≥330º	28 Mean 246º±44 (180–330°)	24*	CS 77% QS 86% at both 12 and 36 months.	CS 82% QS 82% at both 12 and 36 months.	No significant difference CS p=0.96 QS p=0.76
Toschev et al.[22]	MAT in Congenital glaucoma naïve vs after failed surgery	33	**Group 1 PCG naïve:** 23/23 **Group 2 non-naïve/ SCG:** 10/13	0	3**	No info.	No info.	No info.
El Sayed et al.[23]	PCG MAT vs CT	33	19	14	0	No info.	No info.	Mean cannulation MAT 336º±34 vs CT 339º±29, p=0.70
El Sayed et al.[24]	Childhood glaucoma MAT vs CT	30	15 All 360º	15 Mean 323±42º (250-350º)	0	No info.	No info.	No significant difference - Postoperative IOP - Success rates, p=0.200 - Survival times, p=0.500
Shakrawal et al.[25]	PCG MAT vs CT	20	16	4	0	CS 88% QS 94% at 12 months.	No info	Overall (complete + partial MAT) CS 80% QS 90%
Shi et al.[26]	MAT in PCG naïve vs after failed surgery	42	**Group 1 naïve:** 15/20 **Group 2 non-naïve:** 4/22	**Group 1:** 5/20 Median 360º **Group 2:** 18/22 Median 195º	0	No info	Successful IOP control at 12 months. **Group 1:** 80% **Group 2:** 72%	No significant difference IOP reduction complete vs partial MAT, p=0.950 Positive correlation postoperative IOP and MAT extent (r=0.180, p=0.260)
Shi et al.[27]	Childhood glaucoma MAT vs CT	22	19	3 210°, 270° and 300°)	0	No info	QS 100% at 12 months.	No info.
Temkar et al.[7]	PCG MAT vs Trab-Trab	30	24	6***		CS 96% QS 100% at 12 months.	CS 50% QS 67% at 12 months.	Need for medication was higher in the partial MAT, p=0.180
Dao et al.[28]	MAT for aphakic glaucoma and JOAG	23	**Aphakic** 8/13 **JOAG** 10/10	**Aphakic** 5/13 **JOAG** 0/10	Aphakic 4/13 **JOAG** 0/10	No info.	No info.	No info.
Girkin et al.[29]	MAT in congenital glaucoma	11	6	5	0	No info.	No info.	Mean IOP reduction complete MAT 60% vs partial 55%, p=0.570
Girkin et al.[11]	Congenital glaucoma MAT vs goniotomy	11	6	5	0	No info.	No info.	Mean IOP reduction complete MAT 65% vs partial 52%, p=0.090

Table 6. Comparison between complete and partial canalization using microcatheter assisted trabeculotomy. (*) analyzed in a separate third group; (**) excluded from analysis, considered failures; (***) no differentiation between partial MAT and conversion to CT.

Abbreviations: CS: complete success; CT: conventional trabeculotomy; IOP: intraocular pressure; JOAG: juvenile open angle glaucoma; m: month; MAT: microcatheter assisted trabeculotomy; PCG: primary congenital glaucoma; QS: qualified; SCG: secondary congenital glaucoma.